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PINTA

MAL DEL PINTO; CARATE

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HISTORICAL SURVEY

The disease known under the names of pinta, mal del pinto, carate and several other local denominations in South America seems to have existed in the New World for many years before the arrival of the Europeans. The chronicles of the time [1] mention this disease as prevalent in certain areas. Little attention was paid to this disease until Ruiz Sandoval [2] in 1881 and Montoya y Flores [3] in 1898 described certain phases of it and expounded the parasitic theory, reporting on a number of aspergilli and penicilliums as the cause of this dermatosis. For over a quarter of a century authors of books on dermatology and tropical medicine repeated the only known reports, those just mentioned, and consequently pinta remained a more or less rare tropical disease, supposedly produced by fungi. An important contribution was made by Menk,[4] in 1926, who called attention to the fact that a large proportion of the patients suffering from carate in Colombia had positive Wassermann reactions and concluded that carate was in some way related to an old spirochetosis. A further important step of the greatest con-

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1. Pardo-Castello, V.: Skin Diseases in the New World, Arch. Dermat. & Syph. **28**:22 (July) 1933.

2. Ruiz Sandoval, G.: Memoria sobre el mal del pinto, Gac. méd. de México **16**:36, 49, 65, 81 and 103, 1881.

3. Montoya y Flores, J. B.: Recherches sur les caratés de Colombie, Thesis, Paris, no. 25, 1898.

4. Menk, W.: The Percentages of Positive Wassermann Reactions Found Associated with Various Diseases, in Fifteenth Annual Report of the Medical Department of the United Fruit Company, New York, United Fruit Company, 1926, p. 123.

sequence was the announcement by González Herrejón and Pallares,[5] of Mexico, in 1927, that in performing serologic tests (Wassermann) they had obtained positive reactions in nearly 100 per cent of the patients suffering from mal del pinto in Mexico, that no pathogenic fungi were isolated from the affected skin and that this dermatosis was a spirochetosis similar to syphilis and yaws.

Howard Fox,[6] in a visit to Colombia in 1928 and to Mexico in 1930, was unable to obtain any pathogenic fungi from the skin of patients with pinta and agreed with González Herrejón's theory that this disease was a spirochetosis. Fox reported his observations at the Eighth International Dermatological Congress in Copenhagen, 1930.[7]

For several years we had observed in Cuba a number of Negro patients suffering from a dyschromic dermatosis, which was considered a form of dermatophytosis in spite of the fact that pathogenic fungi could not be isolated. When the reports of Menk, González Herrejón and Fox became known to us, we thought that the condition observed in Cuba was similar to the one reported by these investigators, an opinion that was strengthened when the serologic reactions (Wassermann and Kahn) in all our cases proved to be positive. However, having had no experience with the clinical aspects of mal del pinto in Mexico or of carate in South America, we hesitated between considering this disease observed in Cuba as a type of dyschromic syphilis or a clinical form of pinta. These doubts were finally dispelled when Fox attended the meeting of the American Dermatological Association in Habana, in 1932, studied some of the cases presented [8] and thought that they were cases of pinta. In spite of this, several Cuban dermatologists still considered that pinta was a parasitic disease or a form of syphilis as late at 1937.[9] One of us (V. P.-C.) reported a number of cases in 1936 [10]

5. Gonzalez Herrejón, S., and Pallares, M.: Nuevas orientaciones para el estudio del mal del pinto, Hosp. gen. **2**:109 (April-Sept.) 1927; cited by León y Blanco, F.: Nota sobre la evolución histórica de nuestros conocimientos acerca del mal del pinto o carate, Rev. de med. trop. y parasitol., bacteriol., clín. y lab. **6**:289 (Sept.-Dec.) 1940.

6. Fox, H.: Carate (Pinta) as Observed in Colombia, South America, Arch. Dermat. & Syph. **18**:673 (Nov.) 1928.

7. Fox, H.: Mal del Pinto as Observed in Mexico. Its Relation to Carate, read at the Eighth International Dermatological Congress, Copenhagen, 1930.

8. Pelaez, A.: Syphilitic Leukoderma and Keratosis? Pinta? Arch. Dermat. & Syph. **26**:920 (Nov.) 1932. Pardo-Castello, V., and Ibarra, R.: Syphilitic Leukoderma and Keratosis? Pinta? ibid. **26**:921 (Nov.) 1932. Pardo-Castello, V.: Syphilitic Leukoderma (Symmetrical) and Keratosis? Pinta? ibid. **26**:921 (Nov.) 1932; Syphilitic Leukoderma with Atrophy? Pinta? ibid. **26**:922 (Nov.) 1932.

9. Grau Triana, J.: Contribución al estudio de la pinta o carate en Cuba, Arch. de med. int. **3**:125 (March-April) 1937.

10. Pardo-Castello, V.: Pinta o carate en Cuba, Rev. de med. trop. y parasitol., bacteriol., clín. y lab. **2**:667 (Sept.) 1936.

and affirmed the spirochetal nature of the disease, in accord with González Herrejón and Fox. It might be of interest to mention that Fox recognized the first case of pinta in Cuba when attending a meeting of the Cuban Dermatological Society in January 1928.

The final proof of these theoretic assertions came in 1938, when Drs. Grau Triana and Alfonso Armenteros discovered in the lymph of the cutaneous lesions of a patient with pinta a spirochete indistinguishable from that of syphilis and of yaws. The same organism was found in the lymphatic glands. These findings were confirmed by one of us (V. P.-C.) two days later in a personal case in the dermatologic service of the Hospital Calixto García. The discovery of this spirochete in the lesions of pinta was reported by Sáenz, Grau Triana and Alfonso Armenteros [11] in 1938 and again in 1940.[12]

In view of the difficulties of pursuing these studies in Cuba due to the scarcity of patients with this disease, Sáenz decided that a member of his staff should be sent to Mexico, where pinta abounds in the state of Guerrero, Dr. Francisco León y Blanco being selected for this work.

León y Blanco has been in Mexico ever since, and his investigations in Guerrero have led to an entirely new conception of this disease, which we intend to summarize in this article. The spirochete discovered by the Cuban dermatologists was found in nearly every case of mal del pinto in Mexico. González Herrejóñ,[13] Latapí [14] and Gómez Farías [15] have also made recent valuable contributions to the new conception of this disease. In Venezuela, Briceño Rossi and Iriarte [16] have confirmed the

11. Sáenz, B.; Grau Triana, J., and Alfonso Armenteros, J.: Demostración de un Treponema en el borde activo de un caso de pinta de las manos y pies y en la linfa de ganglios superficiales (reporte preliminar), Arch. de med. int. **4**:112, 1938.

12. Sáenz, B.; Grau Triana, J., and Alfonso Armenteros, J.: Pinta in Cuba, Arch. Dermat. & Syph. **41**:463 (March) 1940.

13. González Herrejón, S.: Resumen histórico de las principales ideas etiológicas respecto al mal del pinto, Medicina, México **18**:619 (Dec. 25) 1938; Genesis de la teoría espiroquetosica en el mal del pinto, Rev. de med. trop. y parasitol., bacteriol., clín. y lab. **6**:1 (Jan.-Feb.) 1940.

14. Latapí, F., and León y Blanco, F.: Las lesiones de principio del mal del pinto, Medicina, México **20**:315 (July 10) 1940.

15. Gómez Farías, R.: El mal del pinto, Rev. méd. mil. **2**:5, 1939; Investigaciones del treponema en las lesiones de 500 casos de mal del pinto, ibid. **2**:32, 1939; Algunas nuevas formas del mal del pinto, Pasteur rev. mens. de med. **12**:236 (Dec. 15), 1939; Inoculaciones experimentales del mal del pinto en la ciudad de México, Medicina, México **20**:395 (Aug. 10) 1940.

16. Briceño Rossi, A. L., and Iriarte, D. R.: Consideraciones sobre el estado actual del carate y su distribución geográfica en Venezuela, Caracas, Tipografia Americana, 1939.

spirochetal nature of carate. In Ecuador, León [17] has reported finding the same organism in the lymph of patients with the so-called "blue disease of the Chillos Valley."

In 1938 León y Blanco [18] inoculated himself and other subjects with material containing the spirochete of mal del pinto in Mexico and studied the initial lesion and the early manifestations of the disease which were popularly known in Mexico as *empeines* [19] but which had not been accepted by the medical profession of that country as related in any way to mal del pinto, in spite of the frequency with which the patients claimed that their mal del pinto had started with *empeines*. This may be well understood if one realizes the numerous clinical aspects of these early lesions, resembling syphilids, lesions of psoriasis and dermatophytids and in no way recalling the typical late lesions of pinta.

Further research by León y Blanco [20] has proved the individuality of pinta as a spirochetosis, as he successfully inoculated pinta in patients suffering from syphilis.

GENERAL EVOLUTION OF PINTA

Pinta resembles syphilis and yaws in its general evolution. It begins with an initial lesion exactly at the site of inoculation; this lesion remains as the sole manifestation of the disease for several months, although it grows and spreads peripherally for several inches. After five months or more, signs of dissemination begin in the form of multiple macules or papules, which follow the same type of growth as the initial lesion and in the course of weeks spread to form plaques of red, purple and slate blue, covered with scales or smooth, sometimes syphiloid, sometimes psoriasiform and sometimes trichophytoid. There may be a few lesions covering a small area of skin, or the greater part of the cutaneous surface may be involved. During this stage the serologic reactions, complement fixation as well as precipitation, are positive in about 60 per cent of the cases. The general health is never affected. The lesions remain superficial, although at times they are rather infiltrated, but they never ulcerate or show any break in the epidermis. The mucous

17. León, L. A.: El mal del pinto en el Ecuador, Rev. de med. trop. y parasitol., bacteriol., clín. y lab. **6**:253 (Sept.-Dec.) 1940.

18. León y Blanco, F.: Estudios sobre la etiologia del mal del pinto, la transmisión experimental del mal del pinto de persona a persona, Medicina, México **19**:17 (March 10) 1939; Segunda nota sobre la transmisión experimental del pinto de persona a persona, ibid. **19**:121 (May 10) 1939; Tercera nota sobre la transmisión de mal del pinto de persona a persona, Rev. méd. mil. September-October 1939, vol. 12.

19. León y Blanco, F.: Los empeines en los antecedentes de los pintos, Medicina, México **20**:310 (June 25) 1940.

20. León y Blanco, F.: Cuarta nota sobre la transmisión experimental del mal del pinto de persona a persona, Rev. de med. trop. y parasitol., bacteriol., clín. y lab. **6**:13 (Jan.-Feb.) 1940.

membranes are not affected. The lymphatic glands may be slightly enlarged. There are no subjective sensations in the majority of patients, although a few complain of itching. At this stage the initial lesion becomes indistinguishable from the others.

The clinical picture of pinta may remain as described for several months or more than a year, and then the lesions tend to become dyschromic, acquiring the aspects of the late manifestations well known in Mexico, Colombia, Ecuador, Venezuela and lately in Cuba and thought to be the sole cutaneous manifestations of the disease until 1939. The lesions then tend to be symmetrically situated, especially on the hands and feet, recalling the dyschromia of vitiligo. Palmar and plantar hyperkeratoses are common; areas of atrophoderma may be observed in old infections. The serologic reactions of the blood are positive in practically 100 per cent of these patients.

This last stage of the disease may last for many years, progressing slowly, without apparently affecting the general health of the patient, although changes in the spinal fluid and especially aortic enlargement have been recorded.[21]

Initial Lesion.—According to León y Blanco,[22] the initial lesion appears at the site of inoculation in the form of a minute papule usually surrounded by an erythematous halo between the seventh and the tenth day after inoculation. By the twentieth day the papule appears brilliantly red and raised about 3 mm. above the normal surface of the skin. Sometimes the lesion is an erythematous macule covered with fine scales. Between the thirtieth and the fiftieth day the lesion flattens and appears as an erythematosquamous patch, slightly infiltrated and with ill defined edges. In patients with dark skin, a slate blue discoloration may be observed at this stage, due to accumulations of melanophores. As time goes by, the initial lesion grows peripherally into an oval or rounded patch increasing in diameter to 4 or 5 inches (10 or 13 cm.). Often small papules or macules surround the initial lesion and finally become merged with it, and in this case the outline of the patch may be circinate. Finally, the initial lesion becomes part of the disseminate secondary manifestations and cannot be distinguished from them. Two or more initial lesions may exist and grow simultaneously.

The location of this first manifestation of pinta is usually on the extremities, more often on the lower ones, and occasionally on the face or neck. No case has been reported in which the disease was of venereal origin.

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21. (*a*) Thonnard-Neumann, E.; camacho Moya, J., and Brewster, K. C.: Is Carate (Pinta) a Dermatomycosis? in Nineteenth Annual Report of the Medical Department of the United Fruit Company, New York, United Fruit Company, 1930, p. 101. (*b*) Pardo-Castello.[10]

22. León y Blanco, F.: La lesión inicial del mal del pinto, Rev. de med. trop. y parasitol., bacteriol., clín. y lab. **6**:21 (Jan.-Feb.) 1940.

Early Disseminated Manifestations.—The superficial, disseminated cutaneous manifestations of the disease have been appropriately called pintids by León y Blanco.[23] They may remain unaltered for many months. More often the cutaneous plaques grow slowly, attaining a

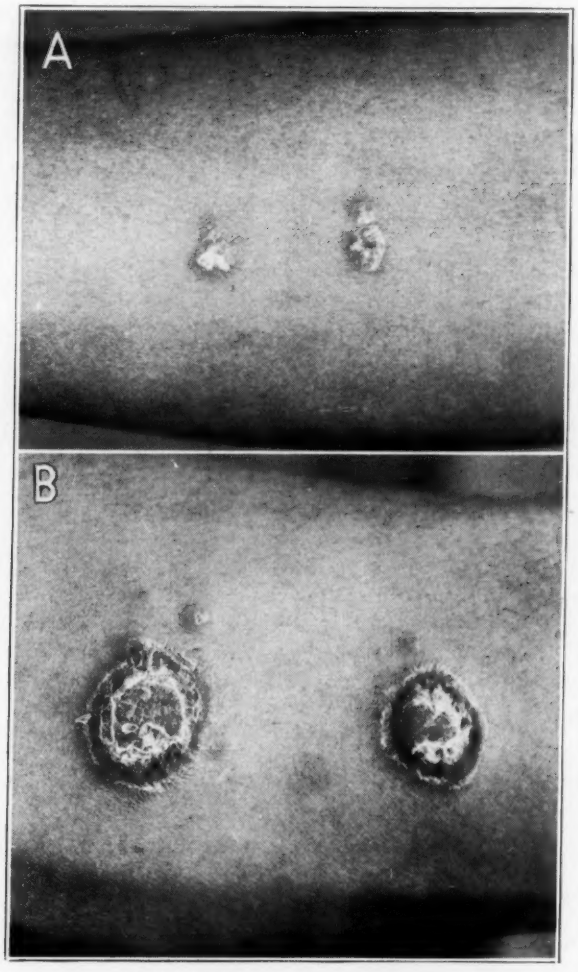

Fig. 1.—Experimental initial lesions of pinta. One lesion was the result of inoculation with spirochetes from a case of Mexican mal del pinto, the other with spirochetes from a case of Cuban pinta. In both lesions the same characteristics have developed forty-six days (*A*) and sixty-two days (*B*) after inoculation. Note the small satellite papules (León y Blanco).

diameter of 5 to 10 inches (13 to 25 cm.) or even more. The so-called *empeines*[19] in Mexico are covered by scales and affect several

23. León y Blanco, F.: Las lesiones de principio del mal del pinto, Rev. méd. mil. **2**:37, 1939.

different types, i. e., psoriasiform, syphiloid, trychophytoid, lichenoid and eczematoid, their outlines being often circinate or ring shaped. The differentiation from leprosy and other inflammatory dermatoses may be difficult. The finding of the spirochete of pinta in these manifestations is easily effected, thus making the diagnosis certain. At this stage the patients may complain of itching. The sensations of pain and temperature at the affected areas are normal, which distinguishes them from the lesions of leprosy.

Fig. 2.—Trichophytoid pintid in Cuban pinta.

The earlier lesions are macules of light pink, but they soon turn dark red, purple or slate color, according to the amount of pigment in the affected skin. When these lesions are scaly they may appear dusty and ashen, the scales being usually adherent and powdery. In some cases the scales are larger and the patches assume the aspect of psoriasis or chronic scaly eczema. These lesions coalesce to form larger plaques.

The site of these lesions may be any part of the cutaneous surface, but most often they are found on the extremities, the bony prominences

and especially the uncovered parts. In the course of several months, as these earlier manifestations pass into the chronic late stage, the location tends to be symmetric, especially on the hands and feet. In older lesions the center may show a certain involution, lighter color and even achromia, the border appearing prominent and darker and advancing peripherally on the normal skin, but slowly, taking several months or even a year to include 1 to 2 inches (2.5 to 5 cm.) of normal skin.

The lesions may be present in different stages of evolution, being pink, red, purple or brown according to the amount of congestion and pigmentation and the color of the normal skin; white persons tend to

Fig. 3.—Mexican mal del pinto (León y Blanco). *A*, erythematosquamous pintids and (*B*) psoriasiform pintid.

show pink, red and brown lesions, while the dark races show purple, blue and slate color. The well marginated border, sometimes polycyclic, is also a frequent feature.

This picture of early pinta is not always so regularly developed and prominent. Undoubtedly there are cases in which the initial lesion as well as the early manifestations are slight, transient or even absent and only the late dyschromic vitiligoid areas are observed, characterized by an extremely slow development without any subjective sensations. This is apparently what happens in many cases in Mexico and in the cases of most of the Cuban patients, who almost unanimously assert that they have not previously suffered from any disease of the skin.

During this early stage of the disease, which may last a year or more, the serologic reactions gradually become positive, and it may be asserted that fully 60 per cent of the patients with this stage of the disease have strongly positive Wassermann and Kahn reactions. The spirochete is always present in the lymph of the affected skin and is easily demonstrable by dark field examination.

Discrete enlargement of the lymphatic glands has been reported, and spirochetes have been observed in the lymph obtained from these enlarged glands.

Fig. 4.—Cuban pinta. *A,* syphiloid lesions on the forearm and typical beginning dyschromic manifestations on the hand, showing transition between early and late lesions. *B,* late manifestations. Notice the mottled pigmentation and leukoderma on the forearm. The triangular area of leukoderma on the wrist is characteristic.

The early lesions of mal del pinto have been described in a masterly manner by Latapí and León y Blanco [14] in Mexico.

Late Dyschromic Manifestations.—These are the best known and most frequently reported of all the lesions of pinta in Cuba. These late manifestations are ones reported also from Mexico and Colombia, occurring on the extremities and causing depigmentation alternating with areas of hyperpigmentation, resulting in a clinical picture resembling vitiligo.

These cutaneous dyschromias are usually symmetrically located on the hands and forearms and also on the feet and legs. Cases in which the disease affected one extremity or affected a hand and a foot on opposite sides have been reported. Palmar and plantar hyperkeratoses of either diffuse or punctate type and with or without the formation of fissures are common in Cuba and rather unusual in Mexico.[24] We encountered a case in which the entire surface of the leg was affected by

Fig. 5.—A Cuban Negro with late manifestations of pinta resembling vitiligo. The lesions were rich in spirochetes. The spirochetes for experimental inoculation (fig. 1) were obtained from this patient (León y Blanco).

the disease in the form of a mass of hyperkeratotic material with dyschromic edges. Follicular keratoses and areas of desquamation have been observed in some cases. In cases of long duration areas of atrophy may be present among the dyschromic zones.

24. León y Blanco, F.: Las queratosis palmares y plantares en el mal del pinto, Rev. de med. trop. y parasitol., bacteriol., clín. y lab. **6**:167 (July-Aug.) 1940.

On the face and trunk the manifestations of late pinta also have the tendency to be symmetrically situated and the arrangement is that of a mottled black and white dyschromia. We have seen lesions on the scrotum coincident with typical manifestations on the hands and feet; the lesions of the scrotum were indistinguishable from those of vitiligo, but the spirochete of pinta was recovered from the lymph of the affected scrotal areas.

In 2 of our cases the mucous membrane of the mouth showed hyperpigmentation, in the form of a triangular-shaped area on the dorsum of the tongue in 1 case and as stippled pigmentation of the cheeks and palate

Fig. 6.—Dyschromia and hyperkeratosis of the soles in Cuban pinta.

in another. Serologic reactions in this late period of the disease are positive in 100 per cent of the cases, and the lymph of the affected areas is rich in spirochetes except in the old, atrophic, burnt-out patches.

Areas of depigmentation in the form of symmetric triangles on the anterior surfaces of the wrists are a common feature. Pigmented lesions may vary from jet black to slate to coffee colored, according to the darkness of the normal skin. In white persons the patches are light brown. The white portions vary from milk white to ashen to yellowish white. The arrangement is usually pepper-and-salt or mottled. The desquamation varies in different persons and in different locations but is usually branny and adherent when present.

Aortic and Cerebrospinal Changes.—Of the 23 cases reported by one of us in 1936,[10] in 5 there were increased globulin values and in 1 positive Wassermann and Kahn reactions of the spinal fluid. Aortitis was reported first by Thonnard-Neumann, Camacho Moya and Brewster [21a] and then by Pardo-Castello [10] and Sáenz, Grau Triana and Alfonso Armenteros.[12]

Of 41 cases studied since then, in 23 the spinal fluid was examined, and in 31 the condition of the aorta was studied clinically and roentgenologically. The ages ranged from 23 to 82, and the duration of the disease varied from ten months to thirty years or more. In 12 cases (52.1 per cent) there were pathologic changes in the spinal fluid similar to those encountered in cerebrospinal syphilis but no clinical mani-

Fig. 7.—Dyschromia and hyperkeratosis of the palms in Cuban pinta.

festations of disease of the central nervous system. In 20 cases (64.5 per cent) there were enlargement of the aorta and thickening of the aortic wall, and although in some of these the age was possibly a factor, in others, in which the ages varied from 36 to 58, pinta was thought to be the possible cause. High blood pressure was present in 8 cases, in 5 of which no aortic changes could be ascertained.

The liver, kidney and spleen were apparently normal in all our cases. Lymphatic glands were enlarged in a few cases, but this enlargement was discrete and we do not believe that it is a prominent feature of pinta. Blood counts were normal in the majority of cases, and in others hypochromic anemia was present, probably due to the presence of intestinal parasites.

Case	Sex	Race	Age	Location of Lesions	Cardiovascular Findings	Serologic Reaction of Blood	Spinal Fluid			
							Cells	Globulin	Kahn-Meinicke Reaction	Lange Reaction
1	M	C	58	Hands, feet, elbow	B. P.: 265/145	++++	0	++	Negative	0122221000
2	F	C	60	Hands, forearms	B. P.: 200/110	++++	2	....	Negative	0000000000
3	M	W	36	Hands, buccal mucosa	Aortitis	++++	5	....	Negative	0000000000
4	M	C	40	Extremities	Aortitis	+++	0	....	Negative	0000000000
5*	F	C	38	Hands, wrists	B. P.: 165/60	++++	0	....	Negative	0000000000
6	M	C	70	Extremities, mouth	Aortitis	++	12	++	++++	2232210000
7	F	C	30	Hands, face, ears	Normal	++++	3	+	++	1222100000
8	M	C	57	Hands, feet	Aortitis	++++	0	....	Negative	0000000000
9	F	C	27	Hands, feet	Normal	++++	0	....	Negative	0000000000
10	M	C	58	Hands, feet, penis	B. P.: 190/110	++++	7	++	++++	1233221000
11	F	C	67	Left hand and arm	Aortitis; B. P.: 240/115	++++	0	....	Negative	0000000000
12	F	C	37	Hands, feet, mouth, vulva (10 months)	Normal	++++	0	....	Negative	0011000000
13	M	C	46	Hands, feet	B. P.: 130/100	++++	6	....	Negative	0002220000
14*	M	W	32	Hands, feet (3 years)	B. P.: 150/90	+++	..	....	.....	.....
15	M	W	52	Hands, feet, mouth, scrotum	Normal	++++	..	....	.....	.....
16	F	C	52	Hands, forearms	Aortitis; B. P.: 160/94	++++	..	....	.....	.....
17	M	C	73	Feet, legs, mouth	Aortitis	++++	5	+	++	0112210000
18	F	C	23	Feet, legs, hands, forearms (early)	Normal	++	5	....	Negative	0222200000
19	M	C	32	Hands, wrists	Normal	+++	10	++	++	1223200000
20	F	C	63	Hand, leg, foot	Aortitis; B. P.: 200/110	+++	..	....	.....	.....
21	M	C	49	Hands, feet	Normal	++++	1	+	Negative	0111100000
22	M	C	72	Left hand	Normal	++++	2	++	Negative	1222320000
23	F	C	52	Hands, feet	Aortitis	++++	..	....	.....	.....
24	F	C	23	Forearms, feet, mouth (early)	Normal	++	5	....	Negative	0022220000
25	F	C	39	Hands, feet	Nomral	+++	..	....	.....	.....
26*	M	C	69	Hands, feet	Normal	++++	..	....	.....	.....
27	F	C	40	Hands, forearms	Normal	++++	..	....	.....	.....
28	M	C	67	Hands, feet, serotum	Normal	++++	..	....	.....	.....
29*	M	C	48	Hands, forearms	Aortitis	++++	..	....	.....	.....
30	F	C	44	Hands, feet	Aortitis	++++	4	+	++	1122300000
31	F	C	43	Hands, feet	Aortic regurgitation	++++	..	....	.....	.....
32	M	W	52	Hands, feet, legs, scrotum	Normal	++++	..	....	.....	.....
33	F	W	28	Hands (1 year); early lesions	Normal	++	..	....	.....	.....
34	M	W	56	Hands, right foot	Normal	++++	..	....	.....	.....
35	M	C	70	Hands, feet	?	++++	..	....	.....	.....
36*	M	W	58	Hands, forearms	Aortitis; B. P.: 150/80	++++	..	+	Negative	0000000000
37†	M	C	52	Hands, forearms, feet (3 years)	Aortic regurgitation	++++	..	....	.....	.....
38‡	F	C	39	Hands, feet, vulva	Normal	++++	..	....	.....	.....
39	M	C	68	Hands, feet	Aortitis	++++	17	++	++++	3444321000
40*	F	C	67	Hands, forearms	Aortitis; B. P.: 210/110	++++	..	....	.....	.....
41	M	C	82	Hands, wrists, feet, legs	Aortitis	++++	..	....	Negative	0000000000

* In cases 5, 14, 26, 29, 36 and 40 there was a history of syphilis.
† Case 37 was that of a Barbados Negro, who also had Hodgkin's disease. The disease had disappeared while the patient was in Barbados.
‡ Case 38 was the only one in which there was a family history of pinta; the patient's father also had the disease.

EPIDEMIOLOGY; EXPERIMENTAL PINTA

Mal del pinto in Mexico and carate in South America are limited to certain regions, especially the river valleys. In Cuba the disease is endemic, but the patients come from the most diverse parts of the country and no "pinta zones" have been delimited. Furthermore, the manifestations of the disease in Cuba are practically limited to the dyschromic type of the late stage, and seldom have the early lesions been observed, the patients usually saying they have not previously had any disease of the skin. The majority of Cuban patients are Negroes, while in Mexico, Venezuela, Colombia and Ecuador persons of the Indian race and mestizos are the most frequent sufferers. The white race is not immune, but evidently the disease is rare in white persons. It occurred in white persons in about 12 per cent of our Cuban cases. Children are often affected in Mexico, but the disease is not transmitted to the offspring. In Cuba the youngest of our patients was 23, but we know of children about 10 years old in cases of some of our colleagues.

The experimental inoculation of pinta and the study of its early manifestations, culminating in the recognition of this clinical entity in its true light, are the results of the excellent work carried out in Mexico by León y Blanco,[18] of the staff of the School of Medicine of the University of Habana, and of the contributing work performed by González Herrejón,[13] Latapí[14] and Gómez Farías,[15] of Mexico.

León y Blanco[20] inoculated himself and 31 other subjects who volunteered for the experiments. Of these, 28 were inoculated in Mexico with material from Mexican patients with typical mal del pinto, and 4 were inoculated in Habana with material from Mexican and Cuban patients with pinta. In the Mexican experiments, 17 patients had no history of syphilis and their serologic reactions were negative; 3 patients were known to have syphilis and had strongly positive serologic reactions; 3 patients had suffered from mal del pinto but had been treated and apparently cured with arsenical preparations, and, finally, 5 patients had active lesions of mal del pinto of the late dyschromic type.

Of the first group, of 17 patients, 14 were inoculated with lymph containing spirochetes from patients with early manifestations of mal del pinto, including the so-called *empeines*. The inoculations were made by depositing the infective lymph on superficial epidermic scratches made with the point of a needle. In 3 other patients the lymph was deposited on the uninjured skin and allowed to dry. In all the first 14 patients initial lesions of pinta developed, but the other 3 remained unaffected, although they were later successfully inoculated by superficial scratching of the skin.

The 3 patients who were known to be syphilitic with positive serologic reactions were successfully inoculated with lymph containing the

spirochete of mal del pinto, and later numerous disseminated cutaneous manifestations of this disease developed. Another person was inoculated with spirochetes contained in the lymph of the lesions of this patient, and pinta developed but not syphilis.

The 3 patients who had suffered from mal del pinto but had recovered were successfully inoculated, a typical initial lesion developing, but disseminated manifestations, or pintids, never appeared. It must be remarked that one of the patients still had strongly positive serologic reactions at the time of reinoculation.

The 5 patients suffering from late dyschromic symptoms of mal del pinto showed no signs of the initial lesion forty-nine days after reinoculation.

These experiments seem to prove the following points: 1. Mal del pinto may be experimentally transmitted from person to person by superficial epidermal inoculation. 2. Syphilis and mal del pinto are two different diseases. Patients suffering from active syphilis may acquire mal del pinto. 3. Mal del pinto confers immunity. Reinfections with the spirochete of mal del pinto are partially successful in the early stages of the disease, but patients with the late dyschromic manifestations cannot be reinfected.

The experiments carried out in Cuba by León y Blanco [25] were made with the purpose of demonstrating that pinta of Cuba and mal del pinto of Mexico were one and the same disease. Four subjects were inoculated with lymph obtained from Cuban cases of pinta from our own hospital service. One subject was suffering from Mexican mal del pinto; the inoculation with lymph from a case of Cuban pinta was successful, and lesions similar to those previously existing on the patient developed at the site of inoculation. The second subject was inoculated with lymph obtained from the first patient, the inoculum resulting in a positive initial lesion after five days. Two other subjects were inoculated with lymph obtained from still another case of Cuban pinta; one of them was known to have syphilis, and the other was an apparently healthy person. The inoculations were performed on the forearms with lymph containing the Mexican strain of spirochete and with lymph containing the Cuban strain. In both subjects typical initial lesions developed with identical characteristics in both inoculums, the resulting manifestations being indistinguishable one from the other. Later these patients were left untreated, and disseminate pintids developed and the serologic reactions became positive.

These experiments prove the following points: 1. Mexican mal del pinto and Cuban pinta are one and the same disease. 2. The spirochetes

25. León y Blanco, F.: Nota sobre la pinta, mal del pinto o carate en Cuba, Arch. Soc. estud. clín. Habana **35**:165 (March) 1941.

obtained from the Mexican and Cuban cases seem to have the same biologic characteristics. The more limited and chronic type of the disease observed in Cuba seems to be the result of peculiarities of the terrain and not of differences in the etiologic agent.

It seems most probable that the mode of transmission of pinta is by local contact with affected persons, since the inoculation can be made in minute and superficial abrasions of the epidermis. The existence of a vector has not been proved, although León y Blanco and Soberón y Parró [26] have recovered spirochetes from the stomach of hippelates flies which had fed on active lesions of mal del pinto and reproduced the disease in 1 case. However, it seems improbable that these insects would transmit the disease by biting, since the spirochetes are delicate organisms, destroyed by the commonest antiseptics, and it is doubtful that they could withstand the action of the digestive juices.

THE SPIROCHETE OF PINTA

The discovery of a spirochete in a Cuban case of pinta by Grau Triana and Alfonso Armenteros, of Habana, Cuba, on Aug. 3, 1938 definitely settled the discussions on the causation of pinta (mal del pinto or carate). The organism was found for the first time in a case of pinta in which there were dyschromic and hyperkeratotic lesions on the hands and feet, so typical of the Cuban cases.

The early lesions are also rich in spirochetes, which are easily demonstrable by dark field examination, silver impregnation of the tissues and Fontana-Tribondau and Giemsa stains in smear preparations.

The lymph is obtained by scratching off the superficial epidermal layers of the affected skin with a sharp curet, holding the skin between the jaws of a surgical clamp and allowing the clear lymph to flow in droplets. The admixture of red blood cells does not interfere with the demonstration of the spirochete, although a clear specimen is preferable. This clear lymph examined under dark field conditions shows variable numbers of spirochetes; sometimes only one or two are seen after long observation, and again some microscopic fields are teeming with the organisms. The late lesions seem to be as rich in spirochetes as the early ones, but the active edges are usually more so. The atrophic areas are as a rule indicative of a burnt-out process and therefore spirochetes are absent. The fresh lymph oozing out of the spontaneous fissures sometimes present on the hands and feet may contain living spirochetes.

The spirochete of pinta is morphologically indistinguishable from that of syphilis and of yaws, although some authors believe it to be much

26. León y Blanco, F., and Soberón y Parro, G.: Nota sobre la transmisión experimental del mal del pinto por medio de una mosca del género Hippelates, Gac. méd. de México **71**:534 (Aug. 31) 1941.

finer. In our experience, specimens are unusually long, much more so than Spirochaeta pallida or Spirochaeta pertenuis, reaching a maximum of 36.8 microns, with an average of 17 microns according to León y Blanco.[27] It has rapid movements across the microscopic field, on its own axis and also bending and unbending; the ends are fine but no flagellums have been demonstrated; the spirals are as regular and about the same in number as those of S. pallida and S. pertenuis. In fresh preparations the organism remains motile from one to six hours, accord-

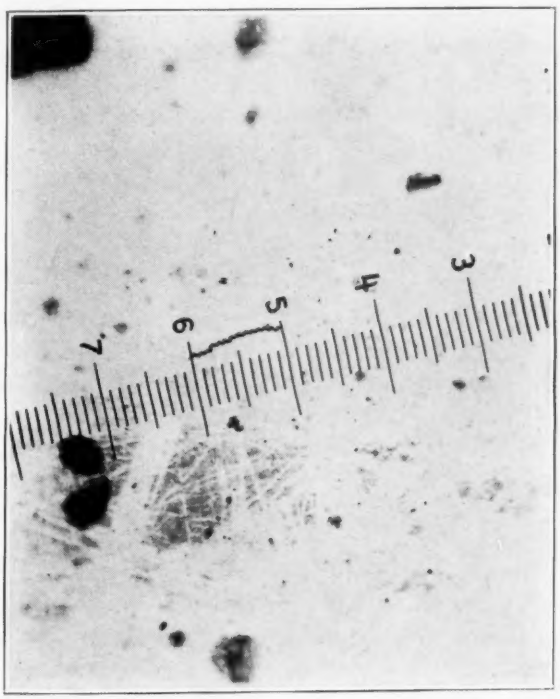

Fig. 8.—Spirochetes of mal del pinto in the lymph obtained from the epidermis (León y Blanco).

ing to the temperature. Heating the specimen at 50 C. for fifteen minutes kills the organisms, but at 40 C. and at 42 C. they survive three and one and a half hours respectively, according to León y Blanco.[28]

In the tissues, the spirochetes are found between the cells of the stratum malpighii, in the hair follicles, in the excretory ducts of the

27. León y Blanco, F.: El treponema del mal del pinto, Rev. méd. mil. **2**:19, 1939.

28. León y Blanco, F.: El treponema herrejoni, Rev. de med. trop. y parasitol., bacteriol., clín. y lab. **6**:5 (Jan.-Feb.) 1940.

sebaceous glands and rarely in the lymphatic vessels of the papillae. León y Blanco has found it in the sweat on the surface of the affected skin.

The first investigator to give a name to the spirochete of pinta was Brumpt,[29] who made a description of it from specimens sent to him from Mexico. Brumpt called it Treponema carateum. Later León y Blanco proposed the name Treponema herrejoni,[28] Pardo-Castello Treponema pictor [30] and Briceño Rossi and Iriarte Treponema americanum.[16]

According to Curbelo, Castro Palomino, Conde and Garzón [31] the spirochete of pinta was cultivated by them anaerobically in ascitic fluid and inoculated successfully in the anterior chamber of the eye of the

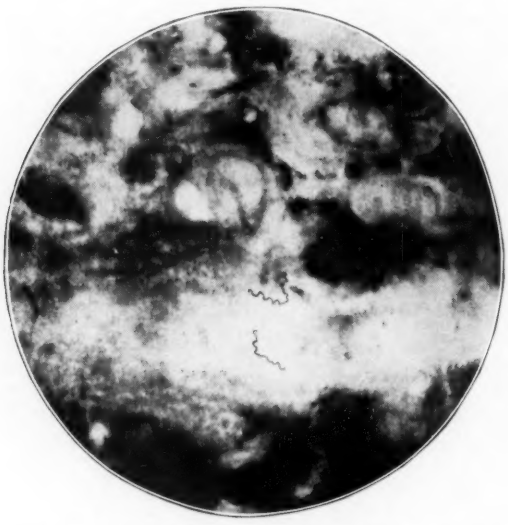

Fig. 9.—Spirochetes of mal del pinto in the epidermis (León y Blanco).

rabbit, causing a keratitis ten days later. Inoculation of the testicles of the rabbits was made, but definite lesions were not observed after seventeen days and no further reports are available from these authors. These findings have not been confirmed by other investigators. León y Blanco [28] stated that the spirochete has not grown in his cultures and that inoculations in animals have failed.

29. Brumpt, E.: Un nouveau tréponème parasite de l'homme: Treponema carateum, agent des carates ou mal del pinto, Compt. rend. Soc. de biol. **130**:942, 1939.

30. Pardo-Castello, V.: El Treponema del mal del pinto, Rev. de med. trop. y parasitol., bacteriol., clín. y lab. **6**:117 (March-April) 1940.

31. Curbelo, A.; Castro Palomino, J.; Conde, E., and Garzón, L.: Ensayos experimentales sobre el agente causal de la pinta encontrado en Cuba, Rev. de cien. méd **1**:134 (Oct.) 1938.

The spirochete of pinta is extremely susceptible to the action of the arsenicals and bismuth. It is impossible to demonstrate these organisms in patients twenty-four hours after one injection of bismuth or after an injection of a small amount of neoarsphenamine or mapharsen.

HISTOPATHOLOGIC CHANGES

The histopathologic changes in the early lesions of pinta have been described by León y Blanco.[32] The initial lesions and the pintids show substantially the same changes and may be described together.

The epidermis is slightly thickened and the papillary processes are elongated; the stratum mucosum shows decided edema and intercellular infiltration of lymphocytes. The pigment is scarce in the basal layer. The corium shows a thick cellular infiltrate composed of plasma cells, lymphocytes and occasional histiocytes and polymorphonuclear leukocytes. Melanophores are especially abundant in the papillary layer. This cellular infiltrate shows predilection for the vicinity of the blood vessels, and toward the edge of the lesion the infiltration occurs exclusively in perivascular patches. The endothelium of the blood vessels is swollen, and the vessel walls are invaded and at times dissociated by the infiltrating inflammatory cells. It is to be noted that even at this early stage the pigment mechanism is greatly disturbed, as shown by the lack of pigment granules in the basal epithelial layer and the presence of enormous numbers of melanophores in the cutis. This explains the slate blue, black or brown of the lesions, according to the color of the patient's skin.

The histopathologic changes in the pintids may show variations according to the clinical type. Parakeratosis and hyperkeratosis may be a prominent feature in the psoriasiform lesions; spongiosis may be present in the trichophytoid types, and microabscesses full of polymorphonuclear leukocytes may be observed at times.

The late lesions are the best known and have been described by various investigators, including Ochotorena,[33] González, Herrejón and Pallares [5] and ourselves. The most important changes are atrophy of the epidermis, absence of pigment in the basal layer, huge accumulation of melanophores in the upper part of the corium, alternate or continuous bandlike infiltration of lymphocytes in the papillary and subpapillary layers and, in cases in which hyperkeratosis is a decided feature, the accumulation of corneous material on the atrophied epidermis.

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32. León y Blanco, F.: Histología patológica de las lesiones cutaneas y de los ganglios linfáticos en el mal del pinto, Rev. de med. trop. y parasitol., bacteriol., clín y lab. **6**:329 (Nov.-Dec.) 1939.

33. Ochotorena, I.: Estudios histológicos y micológicos acerca del mal del pinto, Mexico, Departamento de Salubridad, 1929.

In our cases the atrophy of the epidermis has been an almost constant feature and the patches of melanophores in the subpapillary region a characteristic histopathologic observation. Extracellular grains of pigment may also be noticed in and between the cells of the infiltrate. In the leukodermic patches there are complete absence of pigment, atrophy of the epidermis, disappearance of the papillae and sclerosis of the connective tissue. These are evidently the end of the inflammatory process and represent the final stage, atrophic and cicatricial, of the disease. However, León y Blanco reported on some early vitiligoid lesions with active inflammation in which spirochetes are particularly abundant. We have been able to confirm his observations, especially in a case of vitiligo-like lesions of the scrotum.

In all lesions of pinta it is possible to demonstrate the presence of spirochetes among the cells of the epidermis, especially in the stratum malpighii, by silver impregnation methods.

TREATMENT

The treatment of pinta is the same as that of the two other spirochetoses, syphilis and yaws. The intravenous injection of arsphenamine and the intramuscular injection of a bismuth compound are specific, arsphenamine being, as in syphilis and yaws, more quickly effective than bismuth. Mapharsen has also proved highly effective.

In the early stages, combined treatment with arsenical preparations and bismuth causes the rapid disappearance of the lesions, leaving no trace of their existence. A few weeks after healing the skin seems to be entirely normal.

In the late stages, with alternating hyperpigmented areas and vitiligoid areas, the former disappear almost completely but the vitiligoid patches remain in part, although repigmentation occurs to a great extent. Hyperkeratoses of the palms and soles also respond well to treatment and disappear entirely in the majority of patients. Pigmentary lesions of the mucous membranes also fade considerably and may disappear completely.

The effect of treatment on the serologic reactions is not as good as the rapid involution of the cutaneous manifestations would lead one to expect. The Wassermann and Kahn reactions remain persistently positive in many cases, in spite of the most intensive and prolonged treatment. In others the reactions recede slowly and finally become negative. González Guzmán [34] performed the Kahn exclusion test on the serums of 20 patients with pinta and concluded that positive results are maintained at 37 C. and that a reduction in the positivity is obtained

34. González Guzmán, I.: Contribución para la serología del mal del pinto, Gac. méd. de México **71**:523 (Aug. 31) 1941.

at lower temperatures. Thus the Kahn test is of the same order and type in pinta as in syphilis.

The persistence of the positive serologic reactions in pinta in the absence of active lesions is similar to that reported by one of us (V. P.-C.) [35] in cases of yaws. This makes us doubt the assertion that pinta is easily cured with a few injections of an arsenical preparation, although the pathogenicity of the spirochete of pinta seems to be much less than that of syphilis, and therefore pinta is much less dangerous. Although changes in the spinal fluid, aortic enlargement and high blood pressure have been observed, further observations are needed to evaluate the importance of these findings.

SUMMARY

This article summarizes the recent advances leading to the modern conception of pinta.

Mal del pinto, pinta and carate are one and the same disease, the etiologic agent being a spirochete indistinguishable from that of syphilis and of yaws. This organism has been called Treponema carateum by Brumpt, Treponema herrejoni by León y Blanco, Treponema pictor by Pardo-Castello and Treponema Americanum by Briceño Rossi. Brumpt's denomination has the priority.

Pinta resembles syphilis and yaws in its general evolution. It begins with an initial lesion, followed by disseminate macules and plaques varying in color from pink to red, slate blue, brown and black and ending in a late dyschromic symmetric stage usually affecting the extremities. The complement fixation and precipitation tests for syphilis elicit positive reactions in 60 per cent of the cases of the disease in the early stages and in 100 per cent in the late stages. The lesions are always superficial and never ulcerate. The early lesions sometimes resemble syphilids, trichophytids, psoriasis and eczema. León y Blanco has called the early disseminated lesions pintids.

The appearance of the initial and early lesions is described.

Cardiovascular and cerebrospinal changes have been reported by several authors. In the series of patients studied in this article, 52.1 per cent showed changes in the spinal fluid similar to those found in cerebrospinal syphilis. In 64.5 per cent cardiovascular changes were present, most often aortitis.

Pinta has been transmitted experimentally to man by León y Blanco both in Mexico and in Cuba. His experiences are summarized and the following conclusions drawn: 1. Mal del pinto may be transmitted from person to person by superficial epidermal inoculation. 2. Syphilis and

35. Pardo-Castello, V.: Yaws: Five Hundred Cases Observed in Cuba, Arch. Dermat. & Syph. **40**:762 (Nov.) 1939.

mal del pinto are two separate spirochetoses. Patients suffering from active syphilis may acquire mal del pinto. 3. Mal del pinto confers immunity. Reinfections with the spirochete of pinta are partially successful in the early stages of the disease, but patients with late dyschromic manifestations cannot be reinfected.

Patients inoculated with Mexican and Cuban strains of spirochetes have parallel manifestations of pinta, showing that both organisms have the same biologic characteristics and pathogenicity. The more limited and chronic type of the disease in Cuba seems to be due to peculiarities of the terrain and not to the spirochete itself.

The mode of transmission of pinta is probably by personal contact. It is doubtful that a vector exists capable of transmitting the disease.

The morphologic picture of the spirochete of pinta is studied, and the histopathologic changes in the cutaneous lesions are reviewed. Treatment is also considered.

Forty-one cases of Cuban pinta are reported, especially from the point of view of cardiovascular and cerebrospinal changes.

7-9 Consulado.

TREATMENT OF CUTANEOUS LEISHMANIASIS (ORIENTAL SORE) BY GRENZ RAYS

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AND
F. SAGHER, M.D.
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No data on therapeutic results obtained with infraroentgen rays (grenz rays or bucky rays) in the treatment of leishmaniasis cutis are as yet available. In a preliminary publication [1] 3 cases were reported by us and it was demonstrated that therapeutic effects were, indeed, achieved with this method of treatment; so it seemed worth while to study the question as to what dosage yielded optimal results. The procedure adopted for these studies was to treat several lesions in the same patient separately with varying doses. For this purpose we chose 2 patients, one with thirty lesions on his extremities and the other with seventy. In each of the 2 eight lesions of more or less equal size were treated with different doses and different qualities of rays. For a single sitting the doses varied between 500 and 2,000 r with a half value layer of 0.020 to 0.033 mm. of aluminum. As a result of these experiments, 800 r with a half value layer of 0.027 mm. of aluminum was established as the optimal single dose, which was given one to three times.

As to the treatment of leishmaniasis of the mucous membranes with infraroentgen rays, one report is so far available, which comes from Uruguay.[2] Since we have, however, no access to this article either in the original or in abstract form, it is impossible to compare our results with those reported in that article.

Our therapeutic experiments were conducted on more than 100 patients during the last three years. In 84 of the patients the treatment may be considered as terminated. A total of eight hundred and fifty-three lesions were treated by grenz rays.

To judge the success of the method under consideration, the following factors have to be taken into account: (1) the natural healing tendency

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From the Dermatological Department of the Rothschild-Hadassah University Hospital.

1. Dostrovsky, A., and Sagher, F.: Infra-Roentgen (Bucky) Ray Treatment of Leishmaniasis Cutanea: Preliminary Report, Harefuah, December 1940, vol. 19.

2. Couto Esher, G.: Sobre um caso de leishmanioso mucosa do nariz curado pelos raios de Bucky, An. de oto-rino-laring. d. Uruguay **9**:112-117, 1939.

of the process, (2) the clinical type of leishmaniasis, (3) the duration of the lesions and (4) the site of the lesions.

From a therapeutic viewpoint it is necessary to distinguish between three types of the disease: (1) the nodular, (2) the ulcerative and (3) the relapsing or tuberculoid type. The first two types may be considered as early stages of the disease, while the third constitutes the late stage. The nodular and ulcerative types may heal spontaneously within nine to twelve months, but they may also persist for a greater length of time and merge into the tuberculoid stage. This, however, may appear several years after the process has apparently been completely cured. Then it may again persist for years, even decades.

While the two first types are amenable to the usual therapeutic measures, the third shows no response whatever to any kind of treatment tried up to the present, including chemotherapy. The doses of roentgen

TABLE 1.—*Localization of Lesions in the Early Stages in Seventy-Two Patients with a Total of Eight Hundred and Forty-Two Lesions*

Localization	Number of Patients	Number of Lesions
Face	36	117
Neck, nape of the neck	16	52
Trunk	14	25
Hands	22	43
Forearms	48	208
Arms	28	115
Legs	39	265
Thighs	11	17

rays necessary to influence this condition would be too large to be practicable. The tuberculoid type will therefore be dealt with separately.

In connection with the nodular and ulcerative types the localization of the lesions seems also to be of some significance, which is illustrated in table 1. The regions most frequently attacked are the legs, the forearms and the face, which are usually left uncovered and are therefore particularly exposed to the bite of the phlebotomus,[3] which is generally acknowledged as being the transmitter of leishmaniasis. Such lesions which, as a rule, persist for a year, preponderantly on the lower extremities, get easily infected and constitute a particularly troublesome condition on account of chronic suppuration. As regards the face, the unsightly scars which are left behind are an important factor which has to be taken into consideration in choosing the most suitable method of treatment.

In 7 cases in which the infection had spread through the lymphatic vessels lesions, apart from those at the site of the original infection, and,

3. Adler, S., and Theodor, O.: Further Observations on the Transmission of Cutaneous Leishmaniasis to Man from Phlebotomus Pappatasi, Ann. Trop. Med. & Parasitol. **20**:175-190 (June) 1926.

in 3 cases, swelling of the regional lymphatic glands were observed. Lymphatic dissemination as well as the annular type of lesions are of special significance, for they provide the basis on which recurrences usually develop, and it is an important question to what extent these types are amenable to therapy. Leishmaniasis with secondary infections, such as diphtheria and streptotrichal infection, and the ulcerative type are also of importance, since patients with these conditions may show a strong reaction to the exposure to roentgen rays.

Taking into account the natural healing tendency, a common feature to all the types, apart from the tuberculoid one, we were interested in finding out to what extent the duration of the disease could be shortened

TABLE 2.—*The Morphologic Distribution in Eighty-Four Cases of Leishmaniasis*

Type of Leishmaniasis	Number of Cases
Nodosa	48
Verrucosa	3
Ulcerosa	9
Annularis	3
With lymphatic dissemination	7
With diphtheria	1
With streptotrichal infection	1
Tuberculoides	12

TABLE 3.—*Duration of Lesions and Average Period of Healing in Sixty-One Patients*

Duration of Lesions, Months	Number of Patients	Average Period of Healing, Weeks
1	7	7 to 8
2	23	6 to 7
3	17	7 to 8
4	11	7 to 8
5	3	10

by early treatment; the lesions of long standing had reached the stage of spontaneous healing, so that the treatment was supported by the activity of the protective powers of the organism itself (table 3). In 9 cases the exact period necessary for complete recovery could not be determined, since the patients did not report after the treatment. It is seen in table 3 that the individual periods of recovery varied but insignificantly and that the average was six to ten weeks. In patients whose lesions had been present for five months the average period of healing was ten weeks, although no definite conclusions should be drawn from this fact, owing to the small number of patients in this category.

In 2 of the cases there was complete failure of treatment. In 1 of them the disease had been present for two months and in the other for six months. The lesions healed in 1 case after nine months and in the second after six months, in other words, at a time when they would

probably have disappeared spontaneously. In either case the lesions were on the back of the nose, a localization which is apparently particularly resistant, since other lesions in the same patients which were localized on the trunk showed a more satisfactory response.

No definite relation between the number of lesions and the period of healing could be established (table 4).

In table 5 we are giving a more detailed account of 4 of the cases in which the clinical development as well as the periods of healing were particularly interesting. The 4 patients together had made a trip to the

TABLE 4.—*Relation Between Number of Lesions and Period of Healing*

Number of Lesions	Number of Patients	Average Period of Healing, Weeks
1	14	8½
2 to 5	17	7½
5 to 10	19	7½
10 to 20	5	9
20 to 30	6	8
30 to 50	9	7½
50 to 80	2	7

TABLE 5.—*Comparison of Four Patients Infected with Leishmaniasis* at the Same Time and in the Same Locality*

Age, Years	Number of Lesions	Clinical Type	Localization	Therapy: No. of Treatments	Therapy: Dose	Period of Healing, Weeks	Control Lesions (Left Untreated)
17	7	Annular	Face	2	800 r	7	Still growing (after 2 months)
21	8	Nodular	Extremities	2	700 r	6	
19	1	Ulcerative	Extremities	2	700 r	10	
18	7	Lymphatic dissemination	Extremities	2	800 and 400 r	6	Still growing (after 3 months)

* In all cases infection had taken place two and one-half months previously.

Dead Sea, where they remained for two days. They were all bitten by a phlebotomus and called on us at the same time on account of the cutaneous lesions which had developed. They were of more or less the same age and had been infected at the same time, but different types of leishmaniasis developed. While in 3 cases the parasites could be identified bacteriologically, in 1 the bacteriologic examination, although repeated several times, gave negative results. The period of healing varied between six and ten weeks, although the dosage of rays given in each case did not vary considerably. In each of 2 patients of this party one lesion was left untreated as a control and was found to be still growing after two or three months, while the others in the same patients had long disappeared. Those lesions did not heal before the disease

reached a stage when spontaneous healing was possible. It is therefore highly improbable that immunologic tendencies produced in the lesions under treatment should also have been active in improving the untreated ones.

To form an opinion on the therapeutic effect of the method under consideration, we left some lesions untreated in a total of 6 experimental persons while the others were exposed to grenz rays. In 3 such patients the untreated lesions were still present after three months, and in another 3, after six months. Parasites were identified in 2 cases and were still present after the lapse of six months.

Thus it appears that there is actually a definite influence of the grenz rays on leishmaniasis.

In all cases diagnosis was verified by identification of the organisms, by bacteriologic examination or by cultures, and by intracutaneous tests with leishmania vaccine [4] (in dilution 1 : 1,000,000). In 59 cases the bacteriologic tests gave positive results, while in 13 they gave negative results. In 4 of the 13 cases the organisms could eventually be identified by cultures; so there remained but 9 cases in which the clinical diagnosis alone was decisive, supported, however, by intracutaneous tests. A total of three hundred and twenty-five bacteriologic examinations and forty-five culture tests were made.

In 8 cases careful bacteriologic examinations were also made after termination of the treatment, at intervals of from ten minutes to four weeks after irradiation. In 1 case, rather surprisingly, as early as four days after irradiation no organisms could be detected, although the examinations were repeated several times. In others they did not disappear until the process had been cured clinically. Bacteriologic examination of the scar tissue was also tried in 3 cases but gave negative results. In another case the scar tissue was examined histologically as well, but neither parasites nor the characteristic structure of the tissue could be detected.

TREATMENT

The smallest dose given in one single sitting was 450 r and the largest 1,000 r. The smallest total was 800 r while the largest was 2,400 r; as a rule, however, 1,600 r given in two doses was sufficient. The quality of the rays varied, the half value layer being between 0.020 and 0.033 mm. of aluminum. No difference worth mentioning was noted in the effect achieved with the various qualities of rays; it seemed, however, that the medium type as well as the harder quality was somewhat more beneficial than the soft variety. In general, therefore, we chose a

4. Dostrovsky, A.: The Diagnostic Value of Leishmania Vaccine, Ann. Trop. Med. & Parasitol. **29**:123-128 (July) 1935.

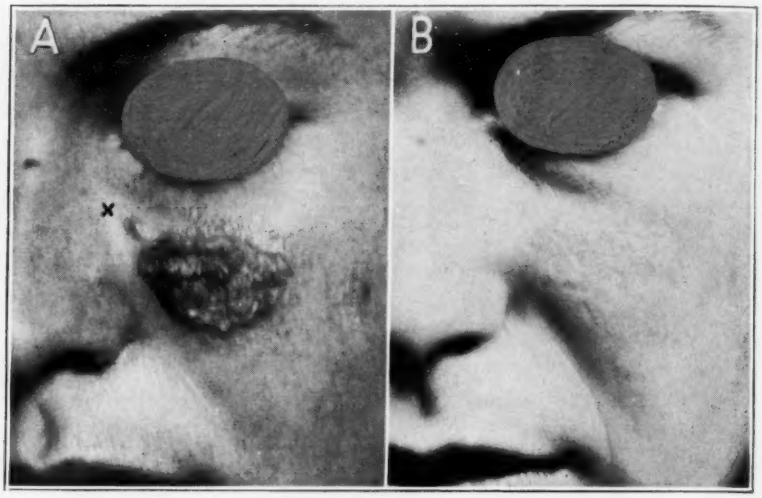

Fig. 1.—*A*, a girl aged 19 with leishmaniasis ulcerosa of three months' duration. *X* indicates bubonulus-like nodules (lymphatic dissemination). *B*, the condition was cured by treatment with infraroentgen rays for ten weeks (total dose, 2,200 r). Note the delicate, shallow scar.

Fig. 2.—*A*, a patient aged 22 with nineteen partly coalescing verrucous lesions of leishmaniasis of three and one-half months' duration. *B*, the condition was cured by treatment with infraroentgen rays for eight weeks (total dose, 1,800 r). Note the slight pigmentation, which later disappeared completely.

half value layer of 0.027 mm. of aluminum, a skin focal distance of 7 cm., 10 milliamperes, 210 volts and 1,360 r per minute.

The cosmetic results were satisfactory. It was particularly astonishing to see how little scarring occurred on the face, and even pigmentation, which was now and then encountered, was much less evident on the face than on the legs.

Follow-up examinations were possible in 42 cases, the shortest period after which the examination took place being three months and the longest two and a half years. No relapses were observed in any of the cases.

A special advantage over the treatment with roentgen rays that should be pointed out is that lesions overlying organs which are radiosensitive (eyelids, thyroid gland and genital organs), as well as the growing organs of children, can also be treated in this way. Since the lesions are most frequently found on the extremities, a possible influence on the bone marrow has also to be taken into consideration. In a hairy region no loss of hair was noted as a consequence of the treatment. Among our patients, 4 had lesions on the eyelids, 6 over the thyroid gland and 2 in the genital region. In none of them did irradiation have a harmful influence.

In order to learn exactly how grenz rays operate, leishmania cultures were exposed to the rays. Although large doses were applied (from 2,000 up to 20,000 r) the cultures continued their undisturbed growth. The gradual disappearance of the parasites from the lesions can therefore be explained only by the occurrence of tissue reactions.

LEISHMANIASIS RECIDIVA

From a clinical as well as a histologic viewpoint, leishmaniasis recidiva is strikingly distinguished from the early stages of the disease, and its response to the therapeutic method under consideration is naturally also a different one. Any kind of therapy which in the early stages may be a great success will be a failure in the treatment of these relapsing conditions.[5]

Leishmaniasis recidiva, which does not occur frequently and is easily confused with lupus vulgaris, is diagnosed only with the help of bacteriologic and histologic examinations, as well as cutaneous tests, although it must be admitted that it was impossible to apply all these diagnostic measures in every patient.

What proportions the destruction of tissue may assume is seen from the photographs of 2 patients (fig. 3), who are, however, still being treated.

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5. Dostrovsky, A.: Relapses in Cutaneous Leishmaniasis, Ann. Trop. Med. & Parasitol. **30**:267-274 (Oct.) 1936.

It is with the greatest difficulty, as in lupus vulgaris, that the parasites are identified in this stage of the disease. Here the culture method yields more satisfactory results. The intracutaneous test with leishmania vaccine nearly always elicits a positive reaction, while control tests with tuberculin (1 : 50,000) invariably give negative results. The histologic aspect is usually that of tuberculoid granulation tissue which is similar to that met with in genuine tuberculous conditions.

We had the opportunity of treating 12 patients with this type of leishmaniasis. Four of them are still being treated at the time of writing and are therefore not referred to here. The remaining 8 are described in table 6.

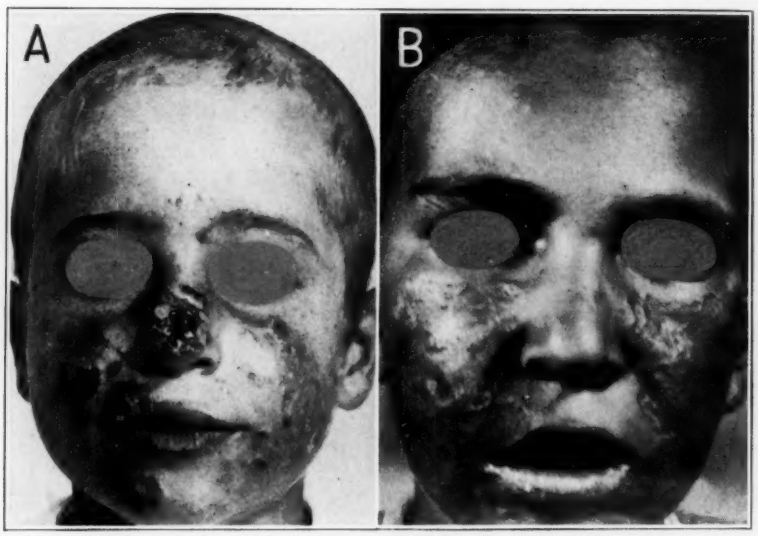

Fig. 3.—*A*, a boy aged 6½ years, from Iraq, with a lesion of six years' duration, which shows various stages of ulcerative, annular and serpiginous types of leishmaniasis and resembles lupus vulgaris. *B*, a 9 year old boy, from Afghanistan, with leishmaniasis recidiva of the face, showing the extensive destruction which may occur in spite of treatment with chemotherapy and roentgen therapy.

The most striking feature in case 1 was the difference in the two kinds of scars, the unsightly one which had formed five years previously where the skin looked as though it had been punched and the other one on the arm which showed only slight pigmentation and no destruction of tissue.

The condition in case 2 represented the serpiginous type of leishmaniasis, which, apparently, is only to a limited extent amenable to any kind of treatment. Two years earlier one portion of the lesions on the face had been treated with roentgen rays. This place showed neither

atrophy nor pigmentation nor depigmentation, although the process itself could not be considered as cured. After our treatment with grenz rays, this lesion as well as the one on the opposite cheek healed completely. Since, however, the patient did not appear again, this could not be checked.

Case 3 was instructive, since it taught us that a perimeter of 3 to 5 mm. must necessarily also be exposed to the rays. In cases in which this precaution was not taken, although the lesions healed in the usual way, new patches appeared at the edges of the scars and even altogether outside the affected area.

In case 8 an exploratory excision was made after the second sitting in order to ascertain the most suitable dose. Some tuberculoid granulation tissue was still found to be present in the depth.

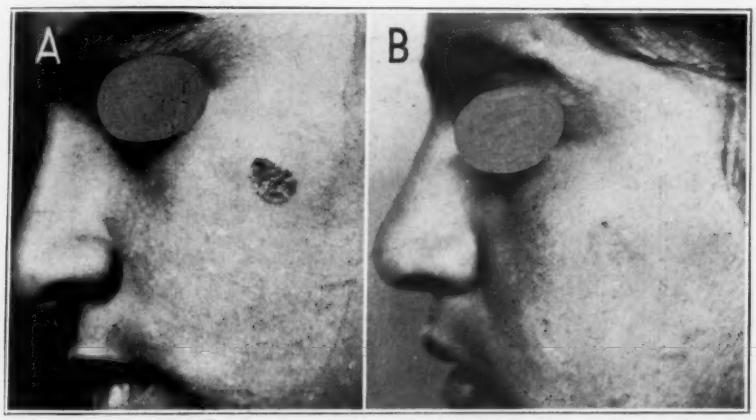

Fig. 4.—A girl aged 12 years, from Palestine, showing (*A*) late stage of leishmaniasis of two years' duration and (*B*) cure after one-half year's treatment with infraroentgen rays (total dose, 6,000 r, soft rays). The black spot in the upper part of the scar is a naevus pigmentosus which has not been influenced.

Our first attempts taught us that the dosage employed with good success for primary lesions was absolutely without result in relapsing conditions. Doses similar to those which as a rule are applied for tuberculosis cutis were therefore tried, the softest kind of rays available being used, moreover. The single doses given were between 1,000 and 3,000 r with a half value layer of 0.02 mm. of aluminum. Irradiation factors were: 7 cm. skin focal distance, 5 milliamperes, 170 volts and 430 r per minute.

As seen in table 6, the total dose varied between 3,000 and 11,000 r. We knew from earlier experience with tuberculosis cutis that this comparatively high dosage made it necessary to use soft rays in order to avoid the danger of superficial ulceration and later disturbances.

TABLE 6.—*Leishmaniasis Recidiva Cured by Infraroentgen Rays*

Case	Age, Years	Duration of Lesions, Years	Number of Lesions	Localization	Bacteriologic Identification	Cultures	Intracutaneous Tests	Histologic Examination	Therapy: Number of Treatments	Therapy: Dose	Period of Healing	Period of Observation	Comment
1	17	4	1	Elbow	+	+	+	Tuberculoid granulation tissue	3	2,000 r	6 mo.	1½ yr.	
2	9	5	2	Face	+	Not made	+	Tuberculoid granulation tissue	4	2,000 r	8 mo.	1 yr.	
3	6	5	3	Cheek	—	—	+	Not made	..	600 to 2,000 r (total, 11,000 r)	18 mo.	2 yr.	
4	12	2	1	Cheek	—	—	+	Tuberculoid granulation tissue	2	3,000 r	6 mo.	10 mo.	Fig. 4
5	11	10	2	Cheek	—	+	+	Tuberculoid granulation tissue	3	2,000 r	7 mo.	10 mo.	After healing, no granulation tissue
6	30	15	1	Nose	—	—	+	Tuberculoid granulation tissue	..	4,800 r	7 mo.	8 mo.	
7	50	1½	1	Cheek	+	Not made	+	Not made	..	3,000 r	4 mo.	.....	Ulcerative
8	8	5	1	Cheek	+	Not made	+	Tuberculoid granulation tissue	2	3,000 r	6 mo.	2 yr.	Pigmented scar

It should be mentioned that in this type of leishmaniasis the lesions usually persist for from one and one-half to fifteen years with no tendency toward spontaneous healing. Their number is usually small, and in the majority of cases they are found on the face. Only in 1 case was the lesion on the elbow.

Leishmania bodies (bacteriologic examinations and cultures) were found in 5 cases. In the remaining 3 cases in table 6 the diagnosis was verified by histologic examination and cutaneous tests, with leishmania vaccine, which elicited invariably positive reactions, while reactions to tuberculin tests (with a dilution of 1 : 50,000, Mantoux) made simultaneously were always negative.

In conclusion we wish to point out that we are fully aware of the fact that the period of observation was too short to give a definite opinion as to the value of this new method of treatment for relapsing leishmaniasis. If we have described these cases at some length, this was done in order to demonstrate that this disease, which, as a rule, stubbornly resists any therapeutic attempt, also shows a beneficial response to the treatment with infraroentgen rays, provided that suitable dosage is chosen.

SUMMARY

Seventy-two patients with leishmaniasis nodosa and leishmaniasis ulcerosa as well as 12 patients with leishmaniasis recidiva with a total of eight hundred and fifty-three lesions were treated by exposure to grenz rays.

For the nodular type the dose employed was two exposures of 800 r with a half value layer of 0.027 mm. of aluminum, while for leishmaniasis recidiva it was from 3,000 to 11,000 r with a half value layer of 0.02 mm. of aluminum.

In cases of the nodular type the lesions disappeared on an average within eight weeks and in cases of leishmaniasis recidiva in six to eight months.

In cases of leishmaniasis recidiva, in which no other kind of therapy has up to now shown satisfactory results, this method of treatment seems to be of particular importance.

Attention is drawn to the advantage of this method over the usual treatment with roentgen rays.

Dr. Gurevitch, head of the bacteriologic department of the Rothschild-Hadassah University Hospital, and Dr. Rabinovitch gave valuable assistance.

BISMUTH ETHYL CAMPHORATE

ITS USE IN TWENTY-SIX CASES OF EARLY SYPHILIS

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The therapeutic value of a drug used in the treatment of syphilis is dependent on certain well known factors, of which the most important are (1) the spirocheticidal effectiveness of the preparation, on which in turn depends the rapidity of the healing of the lesions, (2) the serologic response of the patient and (3) the tolerance of the patient for the drug from the standpoint of immediate and delayed local and systemic reactions. These properties can best be determined in cases of early syphilis (primary and secondary) and in animal syphilis.

Previous studies have been made on the therapeutic effectiveness of bismuth ethyl camphorate. Thurmon [1] found this preparation, which is a liposoluble bismuth salt of ethyl camphoric acid, having 23.47 per cent bismuth (40 mg. elemental bismuth per cubic centimeter), to be an extremely valuable adjunct to the arsphenamines in the treatment of syphilis. In a later study, Thurmon and Benotti [2] found, as judged by the average daily excretion of bismuth in the urine, that bismuth ethyl camphorate administered in 2 cc. doses at seven day intervals maintains the desired level of bismuth in the circulation for a sufficient period to fall within the accepted standards of therapeutic effectiveness. This is in accord with the conclusions of Cole and his co-workers [3] and

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This study was made possible by a grant from The Upjohn Company, Kalamazoo, Mich.

1. Thurmon, F. M.: Bismuth Ethyl Camphorate: Clinical Observations on a New Oil Soluble Bismuth in the Treatment of Syphilis, New England J. Med. **215**:315-321 (Aug. 20) 1936.

2. Thurmon, F. M., and Benotti, N.: Excretion of Bismuth in the Urine of Patients Treated with Bismuth Ethyl Camphorate, Arch. Dermat. & Syph. **42**:1073-1082 (Dec.) 1940.

3. Cole, H. N.; Sollmann, T.; Henderson, K.; Binkley, G. W.; Connors, H.; Cooper, G.; Lover, W. R.; Riechle, H.; Schwartz, W. F.; Seecof, D., and Sullivan, M.: Choice of Bismuth Preparation: Clinical Résumé of Extraction and Retention Studies, Am. J. Syph., Gonor. & Ven. Dis. **23**:143-149 (March) 1939.

of Kolmer, Brown and Rule,[4] who found that preparations so given as to furnish more or less continuous daily urinary excretion of from 2 to 4 mg. or more of bismuth are potentially valuable antisyphilitic agents.

PLAN OF STUDY

Routinely, in this clinic, treatment of all patients with early syphilis is started with an arsenical preparation, given in series of twelve doses. This drug is alternated with a bismuth compound, also given in series of twelve doses. However, for this study the procedure was reversed; the patients began treatment with bismuth ethyl camphorate in 2 cc. doses, for twelve doses, and this was followed by the administration of an arsenical. The experiment concerns itself only with the first course of treatment, namely, that of bismuth ethyl camphorate.

Patients with early syphilis (primary and secondary) in whose lesions Spirochaeta pallida could be demonstrated by dark field examination were chosen for the study. It was planned (1) to give each patient 2 cc. of bismuth ethyl camphorate intramuscularly at seven day intervals; (2) to follow each patient with daily dark field examinations until it became impossible to recover further organisms from the lesions; (3) to note the effect of the preparation on the lesions; (4) to note its effect on the serologic titer, as determined by the quantitative Kolmer-Wassermann and Kline flocculation tests, and (5) to note any toxic effects of the drug. In addition to the aforementioned quantitative serologic tests, the routine Kahn flocculation test was done. Blood for the serologic tests was taken each time a dose of bismuth ethyl camphorate was given.

RESULTS OF STUDY

The accompanying table summarizes the results of this study.

Effect on S. Pallida.—The dark field examination revealed organisms for as long as seven days in only 1 case. The result of the examination in all of the others remained positive for less than seven days; in 3 cases it remained positive for only two days, in 5 for three days, in 6 for four days, in 10 for five days and in 1 for six days.

Healing of the Lesions.—In all of the cases except 3 of primary syphilis with secondary infection, the lesions healed promptly after the beginning of treatment. On the day following the injection little change, if any, could be noted. On the second day definite changes were noted in the majority of cases; this was in the form of less moisture on the moist

4. Kolmer, J. A.; Brown, H., and Rule, A. M.: Studies in the Bismuth Therapy of Syphilis: II. The Therapeutic Activity of Bismuth in Syphilis of Rabbits in Relation to Its Urinary Excretion, Am. J. Syph., Gonor. & Ven. Dis. **24**:415-438 (July) 1940.

lesions. On the third and fourth days this was more evident and there was epithelization of these lesions to some degree; the dry lesions showed definite involution. On the fifth and sixth days the lesions were usually so completely epithelized in most cases that dark field examinations became impractical. On the seventh, eighth, ninth and tenth days only pigmented or depigmented areas were present at the site of the lesions (on the seventh day the patient received the second injection of bismuth ethyl camphorate).

In the 3 cases of primary syphilis with secondary infection the lesions were not treated locally but were permitted to heal spontaneously, so as not to add undue complications to the experiment. The response, as

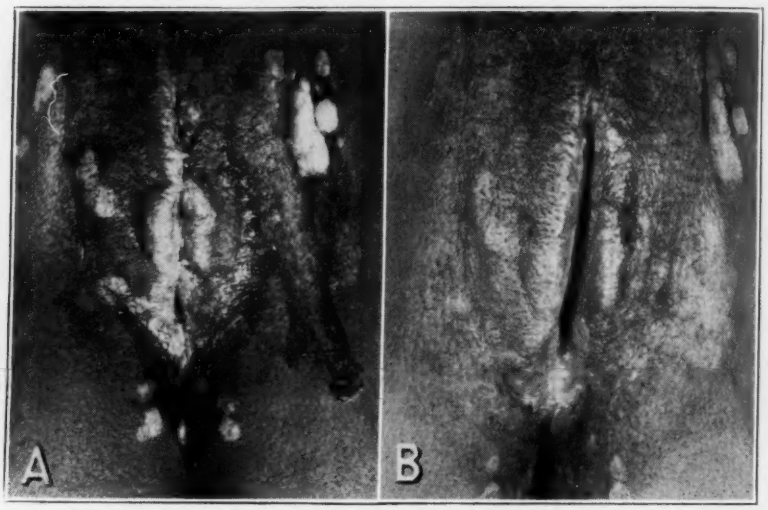

Fig. 1 (case 16).—Condylomata lata of the vulva *(A)* before treatment and *(B)* seven days after injection of 2 cc. of bismuth ethyl camphorate.

shown by the disappearance of spirochetes and the reduction of serologic titer (complete in 2 cases and partial in the third), was satisfactory.

Local and General Reactions.—Only clinical reactions were taken into consideration. All patients tolerated the drug well. Local pain was of minor character, and in no instance was there need for any alarm, either on the part of the patient or on the part of the clinician. General reactions were not encountered. There was no gingivitis or stomatitis.

Serologic Effect.—Twenty-one of the 26 patients received ten to twelve doses of bismuth ethyl camphorate. Twelve of this group of 21 had primary syphilis. In 8 of the 12 the serologic reaction became negative; 1 showed no change, and 3 had considerable reduction of serologic titer. Three of these 12 had negative serologic reactions at the time

Fig. 2.—Annular papular syphilid *(A)* before treatment and *(B)* eleven days after beginning of treatment by two injections of 2 cc. of bismuth ethyl camphorate at seven day interval.

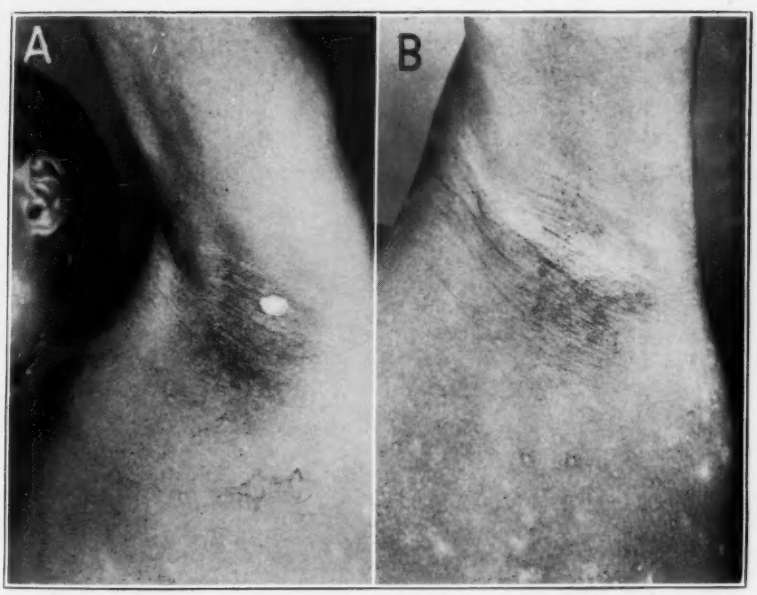

Fig. 3.—Axillary condyloma latum *(A)* before treatment and *(B)* eleven days after beginning of treatment by two injections of 2 cc. of bismuth ethyl camphorate at seven day interval.

Twenty-Six Patients with Early Syphilis (Primary and Secondary) Treated with Bismuth Ethyl Camphorate

Patient and Sex	Race and Age	Diagnosis	Result of Dark Field Examination Positive, Days	Doses of Bismuth Ethyl Camphorate	Period in Which Treatment Was Given, Days	Results of Serologic Tests *			Comment
						At Beginning of Observation	At Second Observation	At End of Observation	
1 ♂	W 19	Seropositive Primary	2	12	74	W: 44444100000 K: 444 Kl:441000	44444200000 444 441000	00000000000 000 000000	Primary lesion secondarily infected; local treatment not used so as not to complicate experiment; lesion healed in 36 days; serologic titer became and remained negative after 10 doses
2 ♂	N 21	Seropositive Primary	3	12	118	W: 00000000000 K: 000 Kl:000000	00000000000 000 200000	00000000000 000 000000	Lesion healed promptly in 8 to 10 days; trace of reagin in Kline test at time of third and fourth treatments; relapses not noted in face of lapses
3 ♂	N 35	Seropositive Primary	3	12	83	W: 44444430000 K: 444 Kl:4444420	44444433200 444 444300	00000000000 000 000000	Lesion healed in 7 days, at which time only depigmentation was present at site of lesion; serologic reactions became negative at time of tenth dose of bismuth ethyl camphorate
4 ♂	N 20	Seropositive Primary	3	12	98	W: 44000000000 K: 000 Kl:444000	44444430000 000 444430	00000000000 000 000000	Lesion completely healed in 9 days; site of lesion marked by area of depigmentation; serologic reaction became negative at time of ninth dose
5 ♀	N 18	Seropositive Primary	3	12	134	W: Positive K: Positive Kl:Positive	44444440000 444 4444410	00000000000 000 000000	Lesion completely healed in 8 days; relapse not noted at any time in spite of long lapses; serologic reaction became negative at time of ninth dose
6 ♂	W 43	Seropositive Primary	4	12	96	W: 00000000000 K: 000 Kl:000000	00000000000 013 000000	00000000000 000 000000	Lesion healed in 6 days; faint trace of reagin found in Kahn test at time of second treatment; serologic reactions were negative at time third dose was given and remained negative thereafter
7 ♂	W 43	Seropositive Primary	4	12	75	W: 00000000000 K: 000 Kl:000000	43300000000 013 440000	00000000000 000000 000000	Lesions healed in 10 days; definite evidence of reagin after first week of treatment; serologic reactions became negative at time eighth dose was given
8 ♂	N 16	Seropositive Primary	6	12	84	W: 43100000000 K: 004 Kl:200000	44443100000 134 400000	00000000000 000 000000	Lesion completely healed in 9 days; definite rise of serologic titer after first dose; serologic reaction became negative at time fifth dose was given
9 ♂	N 21	Seropositive Primary	4	6	56	W: 00000000000 K: 000 Kl:410000	44431000000 034 440000	00000000000 000 000000	Primary lesion secondarily infected; local treatment not used for obvious reasons; serologic reactions became negative at time fifth dose was given; definite rise of titer after first dose
10 ♂	N 19	Seropositive Primary	5	11	71	W: 44444443000 K: 444 Kl:444440	44444442000 444 444420	44431000000 344 441000	Lesion healed in 11 days; very marked decrease of serologic titer
11 ♂	W 24	Seropositive Primary	7	12	108	W: 44400000000 K: 144 Kl:440000	44444100000 444 444000	44400000000 144 440000	Lesion secondarily infected; healed in 24 days; relapse not noted in spite of lapses; definite rise of serologic titer after first dose followed by gradual decline
12 ♂	W 28	Seropositive Primary	4	7	87	W: 44444444300 K: 444 Kl:444444	44444000000 444 444410	44430000000 044 400000	Lesion so extensively healed after fifth day that dark field examination became unsatisfactory; no relapses in spite of long lapses; marked reduction of serologic titer

13 ♀	W 34	Seropositive Primary	3	11	102	W: 44443000000 K: 444 Kl: 444200	44444420000 444 444000	00000000000 014 200000	Lesion so extensively healed after fifth day that dark field examination became unsatisfactory; no relapses in spite of lapses; marked reduction of serologic titer
14 ♀	N 20	Seropositive Primary	5	12	124	W: 44444200000 K: 444 Kl: 430000	44444320000 444 444200	00000000000 000 410000	Lesion completely healed in 8 days; long lapses with no serologic or clinical relapse; marked reduction in serologic titer
15 ♀	N 15	Secondary	2	12	105	W: 44444443000 K: 444 Kl: 444410	44444320000 444 444430	00000000000 000 000000	Lesions so completely healed in 6 days as to make dark field examination impractical; serologic reactions became negative at time tenth dose was given
16 ♀	N 16	Secondary	5	10	201	W: 44444432000 K: 444 Kl: 443000	44444410000 444 444300	00000000000 000 000000	Lesions healed promptly; in spite of very long lapses there has been no relapse
17 ♀	N 20	Secondary	5	7	71	W: 44444420000 K: 444 Kl: 444300	44444430000 444 444000	44430000000 144 444	Lesions so extensively healed in 6 days that further dark field examination was impractical; case disappeared from observation after 7 doses
18 ♀	N 15	Secondary	4	4	95	W: 44444310000 K: 444 Kl: 444300	44443210000 444 420000	44430000000 144 400000	No relapses in spite of long lapses in treatment; marked reduction of serologic titer with only 4 doses; dark field examination impractical after 6 days because of extensive healing of lesions
19 ♀	N 20	Secondary	5	10	104	W: 44444420000 K: 444 Kl: 444100	44444000000 444 441000	44441000000 444 443000	Dark field examination impractical after 7 days because of extensive healing of lesions; definite reduction of serologic titer
20 ♂	N 43	Secondary	4	12	84	W: 444444444321 K: 444 Kl: 4444444442	44444444410 444 44444440	44100000000 444 440000	Lesions so extensively healed in 8 days that further dark field examination was impractical; very marked reduction of serologic titer
21 ♀	N 17	Secondary	5	2	8	W: 44443000000 K: 444 Kl: 444400	44444320000 444 444410	....	Lesions completely healed in 8 days; case was then lost from observation
22 ♂	N 18	Secondary	5	11	104	W: 44444430000 K: 443 Kl: 444000	44400000000 444 444400	32000000000 002 100000	After 6 days dark field examination was impractical because of extensive healing of lesions; very marked reduction of serologic titer
23 ♀	N 18	Secondary	2	10	96	W: 44321000000 K: 444 Kl: 440000	44444000000 444 442000	00000000000 044 410000	Dark field examination impractical after 7 days because of extensive healing of lesions; marked reduction of serologic titer
24 ♀	N 15	Secondary	5	12	210	W: Positive K: Positive Kl: Positive	44444430000 444 444400	00000000000 124 410000	Dark field examination not practical after 8 days because of extensive healing of lesions; marked reduction of serologic titer; relapse not noted in face of several long lapses
25 ♀	N 15	Secondary	5	10	118	W: 44444433200 K: 444 Kl: 4444430	44444200000 444 444300	00000000000 012 400000	Lesions healed promptly; relapse not noted; very marked reduction of serologic titer
26 ♀	N 19	Secondary	5	12	98	W: 44444443211 K: 444 Kl: 4444410	44444431000 444 444440	00000000000 000 200000	Dark field examination became impractical in 8 days because of extensive healing of lesions; very marked reduction of serologic titer as evidenced by 2 plus Kline reaction

* W indicates Wassermann test (Kolmer modification); K, Kahn flocculation test; Kl, Kline flocculation test.

the first injection of bismuth ethyl camphorate was given, but on subsequent testing a trace of reagin was found in the blood of 2 patients and the reagin was definitely present in that of the third. The remaining 9 patients of the group of 21 who received ten to twelve doses of bismuth ethyl camphorate had secondary syphilis. The serologic reactions of 2 of the 9 became negative, and 7 had moderate to considerable reduction of serologic titer.

The remaining 5 patients were lost from observation before the bismuth ethyl camphorate therapy was completed: 1 after two doses, 1 after four doses, 1 after six doses and 2 after seven doses. In this group there were 2 patients with primary syphilis, in 1 of whom the serologic reactions became negative. The other patient with primary syphilis and the 3 with secondary syphilis showed definite reduction of serologic titer. The table shows the serologic responses more vividly.

COMMENT

Irregularity in treatment of some of the patients was a major problem. Lapses in treatment unquestionably predispose to relapses, which in turn inhibit (or prohibit) reversal of serologic reactions. Therefore, the results may not be as good as they might have been had there been no lapses. On the other hand, this one factor (lapses) is of definite value in proving or substantiating the belief that drugs used in the treatment of syphilis should have as one of their properties a resistance-building quality. As is noted in the table, a large majority of the patients were irregular in seeking treatment. One of the patients lapsed for as long as thirty-eight days and another for fifty-six days. In not one instance in the entire series was there evidence of either clinical or serologic relapse. One patient (11), however, failed to show any serologic improvement with twelve doses of bismuth ethyl camphorate given in one hundred and eight days. Therefore, one should accept whatever good results this study shows with reservation, because of the small group of patients. In spite of that, one cannot completely overlook the fact that there were no relapses, which might have been due to chance but, on the other hand, might have been due to the resistance-building quality of bismuth ethyl camphorate.

Obviously, all of the cases cannot be considered in the evaluation of serologic response, but all of them are of some value in consideration of other factors, namely, spirocheticidal effectiveness and healing of lesions. The lesions, as a rule, healed rapidly after the second day of treatment. Since healing is dependent on the disappearance of spirochetes, it is to be expected that there should be some delay in healing. The bismuth is absorbed gradually, and some time must elapse before the systemic concentration is sufficient to produce its maximum spirocheticidal effect. In 16 of the 26 cases the results of dark field examina-

tion became negative in four to five days. In only 2 were organisms present for more than five days; in the remaining 8 the examination revealed organisms for two to three days. When arsenical preparations are used, the results of dark field examination become negative in twenty-four to forty-eight hours. With arsenical therapy, the maximum concentration of arsenic is shortly after injection, and its action is more or less explosive, due to the sudden high concentration. Thurmon and Benotti [2] showed the maximum urinary excretion of bismuth ethyl camphorate, which follows the maximum systemic concentration of bismuth, to take place between the fourth and the sixth day following the injection. This is the time at which the results of dark field examinations became negative in the majority of our cases. The results can be favorably compared with those observed with arsenotherapy, the difference in the time interval being explained by delay in reaching a sufficient concentration.

Lesions healed promptly on disappearance of the spirochetes. Because of a slight delay in the disappearance of the spirochetes, there was undoubtedly a delay in the healing of lesions, but from a clinical standpoint healing seemed to be as rapid as with arsenotherapy.

The serologic response was good in all cases in which a sufficient number of doses was given. Ten patients of the 21 who received from ten to twelve injections of bismuth ethyl camphorate showed negative serologic reactions before or by the time the tenth dose was received. One of the patients in the group, who received less than ten injections, continued to have negative serologic reactions after the fourth dose, but he was lost from observation after the sixth dose. One patient in this same group was lost from observation after the second injection and, therefore, must be disregarded. One patient in the entire series showed no change after twelve injections. The remaining 24 showed either complete reversal or moderate to considerable reduction of serologic titer. The response was more pronounced in the cases of primary syphilis, which leads us to conclude that the shorter the duration of infection the more rapid is the serologic response. This is an observation that was made also in the experiments with massive arsenotherapy of early syphilis by the New York group [5] and by us.[6] Reversal of serologic reactions has required as long as several months in some cases with massive arsenotherapy. Therefore, because of the surprisingly good serologic response in these cases, it may not be out of place to state the belief that

5. Hyman, H. T.; Chargin, L., and Leifer, W.: Massive Dose Arsenotherapy of Syphilis by the Intravenous Drip Method, Am. J. Syph., Gonor. & Ven. Dis. **23**:685-691 (Nov.) 1939.

6. Schoch, A., and Alexander, L. J.: Short Term Intensive Arsenotherapy of Early Syphilis: Preliminary Report, Am. J. Syph., Gonor. & Ven. Dis., to be published.

had it been possible to continue the bismuth ethyl camphorate therapy over longer periods, the serologic reactions of the majority or of all of these patients would have become negative from the bismuth alone.

A temporary rise of reagin was noted in several cases. This is not an unusual occurrence and has been especially pointed out in reports on massive arsenotherapy by Mahoney [7] and by Schoch and Alexander.[6] The rise occurs more often and is more easily recognized in cases in which there is a low initial titer.

SUMMARY

1. Twenty-six patients with early syphilis (14 with primary and 12 with secondary) began treatment with bismuth ethyl camphorate. The observations here recorded are those made during the time the patients received this preparation.

2. S. pallida promptly disappeared from the lesions after institution of treatment.

3. The lesions began healing promptly after the second day of treatment.

4. The preparation is of low toxicity.

5. The large number of serologic reversals speaks well for the therapeutic effectiveness of this drug.

6. Given in 2 cc. doses intramuscularly at seven day intervals, the aforementioned properties were clearly demonstrated.

CONCLUSIONS

This study, made with a small group of patients, shows that bismuth ethyl camphorate definitely possesses the properties of (1) spirocheticidal effectiveness, which in turn leads to prompt healing of lesions, (2) low toxicity and (3) adequacy from the standpoint of serologic response. It may be added that this preparation is also stable and possesses resistance-building qualities.

These qualities, as shown clinically, make bismuth ethyl camphorate, given in 2 cc. doses intramuscularly at seven day intervals, a valuable adjunct to the arsphenamines in the treatment of syphilis.

Parkland Hospital.

1719 Pacific Avenue.

7. Mahoney, J. F.: Massive Arsenotherapy in Early Syphilis by the Continuous Intravenous Drip Method: Résumé of Serologic Observations, Arch. Dermat. & Syph. **42**:262-263 (Aug.) 1940.

MASSIVE ARSENOTHERAPY OF SYPHILIS BY THE CONTINUOUS INTRAVENOUS DRIP METHOD

PRELIMINARY REPORT ON TWO HUNDRED AND SEVENTY-ONE PATIENTS TREATED WITH AN ARSENOXIDE PREPARATION

FLORENCIO PRATS G., M.D.

LUIS INFANTE VARAS, M.D.

AND

ESTEBAN HARASZTI, M.D.

SANTIAGO, CHILE

The enormous interest which has been aroused by efforts to achieve a rapid cure of syphilis warrants recapitulation of the experiences in Chile.

PATIENTS TREATED

Up to Oct. 20, 1941, 233 patients were treated by us. This publication deals at length with only the first 111, whose period of observation extended up to seven months.

Of the 111 patients, 70 were males and 41 females.

The age of the patients varied from 15 to 40 years, 2 being 15 years of age, 36 between 16 and 20, 57 between 21 and 30 and 16 between 31 and 40.

Fifty-four patients were addicted to the use of alcohol, in different degrees, and 68 used tobacco.

Seventy patients gave a previous history of venereal disease, 39 of gonorrhea, 19 of chancroid and 12 of lymphogranuloma venereum.

Chronic alcoholism of severe degree was present in 19 patients. Sixteen patients had chronic complaints of gastrointestinal nature, which suggested some hepatobiliary disturbance. In 11 there was a definite history of allergic disease, urticaria, asthma or eczema. Nine patients suffered from chronic tonsillitis, 2 from duodenal ulcer and 1 from idiopathic epilepsy. Five patients had pulmonary tuberculosis, which was inactive but not longer than four years in duration.

Translation by Dr. William Leifer, New York.

The material presented here was communicated to the Medical Society of Chile, in joint session with the Chilean Society of Dermatosyphilology, on Oct. 17, 1941.

Dr. F. Prats G., is Chief of Section C of the Hospital San Luis de Santiago; Dr. L. I. Varas is Chief of the Section of Clinical Control, and Dr. E. Haraszti is from the Bacteriologic Institute of Chile.

Two pregnant women were treated, 1 in the third and the other in the fourth month of gravidity. None of the women was menstruating at the time treatment was begun, although 7 did begin to menstruate during the course of therapy.

The original North American investigators recommended their method for the treatment of early syphilis. We appreciate that this restriction of the method would lead to the highest expectation of satisfactory therapeutic results. However, in view of the enormous amount of syphilis in Chile, we have treated patients with old infections as well as those with new infections, with the objective of controlling infectiousness as completely as possible.

Of the 111 patients, 10 had seronegative primary syphilis, 16 seropositive primary syphilis, 76 early secondary syphilis, 2 late secondary syphilis and 7 latent syphilis.

Two of our patients had a concurrent chancroidal infection and 2 others active lymphogranuloma venereum. It is important to recognize the presence of other venereal diseases so that the patient may be properly treated for them after termination of the arsenotherapy. Also, the patient should be told of the complicating infection, so that he will not lose heart when his lesions do not completely respond to the antisyphilitic treatment.

DRUG AND DOSAGE EMPLOYED

The arsenical used by us is the hydrochloride of arsenoxide (oxiarsolan), prepared by the Bacteriologic Institute of Chile. This drug has been used by us in routine treatment, in a comparative manner with mapharsen. It was only when we had so convinced ourselves of its low toxicity and high therapeutic potency that we employed it in massive dosage.

For the first 111 cases we had fixed as our total standard dose for the five day period 1.2 Gm. for men and 0.8 Gm. for women. Subsequently, because of the excellent tolerance of the first 41 women treated, we established doses of 0.8 Gm., 0.9 Gm. and 1.0 Gm. for women, in relation to their weight.

Of the 70 men treated, 56 received 1.2 Gm., 4 received 1.18 to 1.19 Gm., 5 received 1.02 to 1.12 Gm. and 5 received less than 1.0 Gm. Of the 41 women treated, 36 received 0.8 Gm. and 5 received 0.74 to 0.78 Gm. Thus, 106 patients (95.5 per cent) received what we considered full dosage, while 5 men (4.5 per cent) received inadequate dosage, or less than 1.0 Gm.

The solvent first used was an isotonic solution of dextrose prepared by fractional sterilization. Because of the general reactions observed, physiologic solution of sodium chloride was substituted. While there

was a notable diminution in the intensity of the reactions, there was an increase in the incidence of pain in the arm, and this solvent was then abandoned. At present we are using isotonic dextrose solution sterilized by passage through a Berkefeld filter.

MANAGEMENT OF PATIENTS

Before treatment every patient was thoroughly examined by the hospital internist, Dr. González Salvatierra. His great experience in the study of toxicologic phenomena due to the arsphenamines is a guarantee of the completeness and objectivity of our report on this score.

All patients had a complete blood cell count, estimations of the nitrogen content of the blood and icteric index and bilirubin studies before treatment was begun. Each day careful urinalyses were made and the blood pressure was recorded. The temperature and pulse were noted hourly during the treatment.

There was no special preparation for treatment, except for a soapsuds enema the evening before treatment.

The therapeutic procedure was begun in the morning before ingestion of food. One and a half to two hours later the patient received coffee, with or without milk. At midday he was served a cup of broth. In the afternoon a light lunch was given, consisting of a cup of broth, cooked rice or vermicelli, a vegetable omelet, about 150 Gm. of meat, roasted or fried in oil, a fresh vegetable salad and some fruit. During the day sweet drinks and lemon juice in abundance were consumed.

TOXIC EFFECTS

The toxic effects are divided into incidents, of a less important character, and accidents, which have greater significance.

Incidents comprised those of a general nature, which included fever, vomiting, headache, abdominal pain and diarrhea; cutaneous reactions, which included erythemas and herpes simplex, and local reactions, which included pain in the arm, phlebitis and cellulitis.

Considered as a whole all these incidents have a toxicologic aspect. Nevertheless, the influence of the syphilitic infection cannot be negated as a factor in their development. Thus, the primary fever, occurring the first day, was undoubtedly a manifestation of the Herxheimer reaction. No one can doubt this when there was seen conjointly with the fever a congestion of the cutaneous lesions. The other incidents of the first day might well be considered of similar character, but it could be argued that the first day is the most appropriate time for toxic incidents, since it may require three or four days for the body to become accustomed to the drug.

Of great interest is the differentiation between the two types of erythema noted. On the first day, after about six hours of treatment, we noted in 14 patients a roseolar erythema, certainly suggestive of a Herxheimer reaction. This we called acute precocious arsenical erythema. The secondary morbilliform erythema has a different interpretation. It appears customarily on the seventh day and corresponds exactly to the erythema of the ninth day of Milian (seen in routine treatment). The latter definitely is of toxic significance.

Primary fever, seen only on the first day, occurred in 64 patients (57 per cent). Secondary fever was noted in 89 patients (80 per cent). Vomiting occurred in 78 patients (70 per cent), headache in 35 (31 per cent), abdominal pain in 10 (9 per cent) and diarrhea in 11 (9.9 per cent). Pain in the arm at some time during the course of treatment occurred in 103 patients (92.7 per cent), and some degree of phlebitis was seen in approximately 90 per cent of the patients. Cellulitis was a rare occurrence.

What we have called acute precocious arsenical erythema, and what is probably a Herxheimer reaction, was seen on the first day in 14 patients (12.6 per cent). The secondary morbilliform erythema, analogous to the Milian reaction, was encountered in only 8 patients (7.2 per cent).

The great frequency with which we have observed these incidents, especially fever and vomiting, is in sharp contrast to the rarity of more important accidents.

Treatments were given with different amounts of solvent and in varying periods of time. It was found that the most favorable conditions were obtained by dissolving the full daily dose (0.24 Gm. for men and 0.16 to 0.2 Gm. for women) in 2,000 cc. of filtered dextrose solution. This quantity was allowed to flow in in a period of ten hours. In this manner, pain became negligible, although the other incidents were not appreciably affected.

An effort was made to correlate the toxicologic effects with the clinical condition of the patient, that is, to determine whether chronic alcoholism, hepatobiliary disturbances, allergic diseases, etc., influenced the incidence of toxic effects. It was found that this group of patients had approximately twice as much secondary morbilliform erythema (Milian) as the group without antecedent nonsyphilitic disease. This was the only difference of importance between the two groups. This would seem to indicate that massive arsenotherapy can be given to patients with visceral disease when the visceral lesions are not of great extent or severity.

Accidents of greater import were noted in a number of patients. These included a syndrome termed by us lipothymia and also precordial

oppression, arsenical dermatitis and polyneuritis. The cases in which such accidents occurred will be described in some detail.

Lipothymia was encountered in a single patient, a healthy man of 23 years, with a history of urticaria and eczema. He was admitted because of secondary syphilis, of about six months' duration, and had received previously a series of injections of neoarsphenamine. On the first day, about four hours after commencement of treatment, he complained of clouding of vision, after which he had a syncopal attack with momentary loss of consciousness. He had received up to that time 0.16 Gm. of the arsenoxide preparation. Treatment was suspended; epinephrine was administered, and the patient responded rapidly and completely. The following day his condition was found to be excellent and the therapy was again started. In about the fourth hour of treatment, after the administration of 0.18 Gm. of the drug, the patient complained of clouding of vision and weakness, but there was no loss of consciousness. Treatment was suspended, and he recovered promptly. He remained under observation and was subjectively and objectively completely well. He protested because treatment had been stopped.

Precordial oppression was observed in 2 patients. In one, it was slight and transitory and disappeared spontaneously, and there was no interruption of therapy. In the other, there were additional complicating factors, and treatment was discontinued. The latter, a man 31 years of age, was in good physical condition. He had a florid secondary syphilis. The first day he received 0.24 Gm. of the arsenical in 1,000 cc. of physiologic solution of sodium chloride in four hours. On that day he showed lacrimation, abundant nasal mucous secretion and acute precocious arsenical erythema (Herxheimer). The second day his condition was excellent and he was given the same dose as he had received the preceding day. About two hours after termination of therapy, he complained of precordial oppression of moderate intensity. The third day he received the same dose of the drug. Again, about two hours after finishing treatment, he complained of precordial oppression, and later an urticarial eruption developed. Treatment thereupon was definitively suspended, and the patient made a complete and rapid recovery from his symptoms.

Dermatitis was seen in a single patient. It seems to us an exaggeration to classify this patient's condition among the accidents, because of the doubtful relation of the eruption to the arsenical. The patient was a man of 33, in excellent physical condition, suffering from early latent syphilis. He had received previously some routine treatment. The eruption appeared eighteen days after termination of the massive arsenotherapy. At first the differential diagnosis wavered between pityriasis rosea and seborrheic eczema. Subsequently the condition took on aspects more

characteristic of an eczema. It cleared up in about three weeks and during this time never resembled true arsenical erythroderma.

Polyneuritis was noted in 3 patients. Two of these complained of slight pain in the legs and principally of a sensation of itching of the soles. The symptoms cleared up in about seven days. The third patient had more severe symptoms but was never confined to bed because of them. His complaints completely disappeared in approximately two and a half months. He had a history of chronic severe alcoholism, and this undoubtedly contributed to the polyneuritis.

In all, 233 patients have been treated by us without a single fatality. We did not encounter a single instance of jaundice, arsenical erythroderma, hemorrhagic encephalopathy, blood dyscrasia or atrophy of the liver.

In addition to the 233 patients treated by us, there were 23 treated by Figueroa and Giacaman and 15 treated by Weinstein and Barría, making a total of 271 patients treated with the arsenoxide preparation in Chile up to October 1941. In this entire group there was not a single serious complication or fatality.

Before treatment was begun with the hydrochloride of arsenoxide (oxiarsolan), 382 patients were treated by various investigators in Chile with neoarsphenamine in varying dosage. In many instances the concentrated dose technic of Tzanck was employed. Of this group, 6 patients (1.57 per cent) had a fatal outcome. It was because of this and also because of the favorable experiences of Leifer, Chargin and Hyman [1] wtih mapharsen that our later patients were treated with arsenoxide.

INTERRUPTIONS OF TREATMENT

Treatment was interrupted temporarily when there was a rise in temperature to above 39.5 C. (103.1 F.). The deficiency in the amount of the drug was made up by increasing the dose on subsequent days. Such transitory interruption of treatment occurred in 25 cases. In 13 of these the full dose could be administered in the following days; in the remaining 12, because of repetition of incidents, the dosage was less than planned.

Treatment was completely interrupted and discontinued in 3 patients: the one who suffered from lipothymia, the one who had severe precordial oppression and one who had prolonged fever. The last-mentioned patient had considerable pyuria and phimosis, which might have been at least partially responsible for the febrile picture. In addition to these 3 patients, there were 4 others who refused to continue treatment because of severe pain in the arm. They were being treated with physiologic

1. Leifer, W.; Chargin, L., and Hyman, H. T.: Massive Dose Arsenotherapy of Early Syphilis by Intravenous Drip Method, J. A. M. A. **117**:1154 (Oct. 4) 1941.

solution of sodium chloride as the solvent, and this undoubtedly accounted for the pain. These 4 patients received from 0.72 to 1.12 Gm. of the arsenoxide preparation.

TOLERANCE AND SPECIAL PHYSIOLOGIC CONDITIONS

It has always been our practice in routine treatment to suspend the administration of arsphenamine during menstrual periods. Of the 41 women treated by massive dosage, 7 began to menstruate during the therapeutic regimen. The first of these 7 patients began to menstruate on the first day of treatment, and it was decided to discontinue the therapy. However, it was begun again two weeks later and carried through to completion. For the remaining 6 patients, treatment was not interrupted because of the onset of menstruation and was carried out without untoward incident.

Two pregnant women were treated, one in the third and the other in the fourth month of gravidity. Both completed treatment uneventfully. The patient who was four months gravid aborted a month after termination of therapy, after severe physical effort. The other patient is still under observation at the time of writing and in excellent condition.

It is our opinion that treatment should not be begun when a woman is menstruating but that treatment need not be interrupted if the menses comes on during its course.

THERAPEUTIC RESULTS

Spirochetes disappeared from the lesions during the first twenty-four hours, and in the greatest number of cases the results of dark field examination were negative between the fifth and the eighth hour after commencement of treatment.

Cicatrization of the lesion depended on the type of lesion. The large infiltrated or gangrenous chancre healed in an average of ten days. Erosive lesions, of a more superficial type, healed in five or six days. The papular secondary syphiloderms disappeared in variable periods. Enlarged inguinal lymph nodes diminished in size slowly and in many instances were still palpable after several months.

The clearing of the serologic reactions occurred between the second and the fifth month. The Wassermann reaction cleared faster than the Kahn. Serologic studies were conducted by Dr. Eduardo Dussert J., and the results were as follows:

Total number of patients treated	111
Patients observed less than two months.....	42
Patients observed and reported on.....	69

Patients with seronegative primary syphilis	9	
Negative reactions after treatment.....	9	(100 per cent)
Patients with seropositive primary syphilis	11	
Negative reactions after treatment.....	9	(82 per cent)
Almost negative reactions after treatment	1	(9 per cent)
Relapse or reinfection after treatment....	1	(9 per cent)
Patients with secondary syphilis	44	
Negative reactions after treatment.....	32	(73 per cent)
Almost negative reactions after treatment	9	(20 per cent)
Persistently positive reactions after treatment.....	1	(2 per cent)
Relapse or reinfection after treatment....	2	(5 per cent)
Patients with latent syphilis	5	
Negative reactions after treatment.....	5	(100 per cent)

The total number of patients observed in the seven month period was 69. At the end of the seven months 55 (80 per cent) gave negative reactions and 10 (14 per cent) almost negative reactions. In 4 (6 per cent) the treatment was considered a failure.

The longest period of observation of these patients, seven months, is too short to permit one to draw any final conclusions. It can only be said that from the figures given approximately 94 per cent of the patients were proceeding in a satisfactory manner.

The 4 patients whom treatment did not benefit included one whose serologic reactions of the blood remained persistently positive up to the fourth month of observation. The other 3 had cutaneous lesions material from which showed organisms on dark field examination subsequent to treatment. The condition in 2 of these might well have been a reinfection. However, since the essential criteria requisite for such a diagnosis were lacking, we classed their conditions as infectious relapses.

SUMMARY AND CONCLUSION

The hydrochloride of arsenoxide (oxiarsolan), prepared by the Bacteriologic Institute of Chile, has been employed in the massive dose treatment of syphilis by the continuous intravenous drip procedure.

We have treated a total of 233 patients, and 38 more were treated under our observation in Chile.

The average dose for men was 1.2 Gm. and for women 0.8 Gm. in the five day treatment period.

The most satisfactory diluent was dextrose solution sterilized by passage through a Berkefeld filter, 2,000 cc. being used for the daily dose, delivered in a ten hour period.

There was not a single serious complication in any of the 271 cases, and there was no death.

Two pregnant women were treated without any untoward incident.

The immediate therapeutic response was excellent, results of dark field examinations becoming negative in the first twenty-four hours and lesions healing rapidly.

Of 69 patients who were followed up to seven months, 55 (80 per cent) achieved and maintained completely negative serologic reactions of the blood, 10 (14 per cent) had almost completely negative serologic reactions and in the cases of 4 (6 per cent) the treatment was considered a failure, because of persistently positive serologic reactions in 1 and infectious relapse in 3.

We are highly encouraged by our preliminary results and are continuing with the procedure on a more extensive scale.

MASSIVE ARSENOTHERAPY IN EARLY SYPHILIS

REPORT OF SIXTY CASES IN WHICH NEOARSPHENAMINE WAS GIVEN

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Since 1938 we have treated 60 syphilitic patients with neoarsphenamine in massive doses by the drip method. This paper refers chiefly to the immediate results of the treatment, as no follow-up studies have been made. The small number of reactions found in this series is worthy of mention.

Our technic is somewhat different from that followed by other authors. We inject by the drip method 1.5 Gm. of the arsenical dissolved in 250 cc. of double-distilled water. This requires about four hours. The injection is given on three consecutive days, a total amount of 4.5 Gm. of neoarsphenamine in 750 cc. of water being administered. A week after the last treatment a dose of 0.9 Gm. of the drug in 10 cc. of water is injected by the syringe method. The total amount of neoarsphenamine is then 5.4 Gm.

The 60 patients were all men varying from 22 to 35 years of age. Three of them had primary lesions. With the exception of 1, who had latent syphilis in the early stage, all the others had secondary syphilis, with lesions of the skin and mucous membrane. Two of them presented cutaneous relapses. In all cases the dark field examination showed Spirochaeta pallida and the Wassermann reaction of the blood was positive.

The patients were kept in bed from the time of admission to the hospital till two days after the last injection. Daily intramuscular injections of liver extract were given. Before the treatment was started each patient was carefully examined so that any possible contraindication for the method of therapy might be detected. Complete blood counts and urinalyses were performed. General tonics, such as caffeine, strychnine and adrenal cortex extract, were administered when believed necessary. Many patients received sodium thiosulfate by mouth. We

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believe this drug to be a preventive of and a remedy for headaches and vomiting. During the days of the treatment the patients received a light diet, consisting mostly of vegetables with no meat. No meal or even ingestion of water was allowed until two or three hours after the end of the daily treatment.

Our observations confirm those of other investigators of this subject. Dark field examination of material from the lesions failed to show S. pallida after twenty-four hours. The same kind of examination of material obtained by aspiration from the regional lymph nodes also showed no organisms.

The improvement of the cutaneous lesions was striking. The macular eruptions disappeared in less than three days. The papular and moist lesions dried and became pigmented in the same period; they were entirely healed by the eighth day. The vegetating and ulcerating lesions were slower in their response to treatment. They started to show involution on the fifth day and did not heal entirely until the twelfth or fourteenth day. The response of the primary lesions to treatment was also rapid. On the third day the surface of the ulcer showed granulation tissue, covered by an adherent thin crust. The infiltration of the lesion and the adenopathy also improved rapidly.

Few reactions were noticed during the treatment. They consisted mostly of headaches for two or three hours, appearing about one hour after the first two treatments and rarely after the third one. Headaches were found in 15.5 per cent of the cases. Mild circulatory disturbances, some of them due to small faults in the technic and to a decrease of the blood pressure, were noticed in 8.6 per cent. They were controlled easily with ordinary stimulants.

Elevations in temperature were noticed in 8.6 per cent. They were usually small, 1 degree C. (1.8 degrees F.), and were preceded by chills.

Vomiting was rare and occurred mainly when the patient had taken fluids or food too soon after the treatment.

In 1 of the last patients of our series polyneuritis developed with severe paresthesias of the extremities which confined him to bed and prevented the use of his arms. This accident appeared about one week after the last treatment. During this interval the patient had a severe follicular tonsillitis followed by a generalized pyoderma.

Two patients who failed to recover under treatment with neoarsphenamine and arsenoxide in the regular dosage showed great improvement with the drip method.

In our small series the tolerance to massive arsenotherapy by the drip method is better than that to the regular method of treatment.

SUMMARY

Sixty men with syphilis in the early stages were treated with neoarsphenamine given in massive doses by the drip method for three days followed by one injection of the same drug (0.9 Gm.) one week later. The total dose administered during the treatment was 5.4 Gm. The immediate results are recorded. Only a small number of reactions were noticed. In 1 case polyneuritis was observed.

Dr. Orlando Cañizares translated this paper.

SPECIFIC CUTANEOUS LESIONS IN CHRONIC MYELOID LEUKEMIA

CLINICAL SIGNIFICANCE

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Myeloid leukemia with specific cutaneous lesions is a relatively rare condition. In 1934, Hollander, Kastlin, Perman and Schmitt [1] reviewed the early literature and reported 14 unquestionable cases of chronic myeloid leukemia with cutaneous manifestations. They added another case. Since then, additional cases have been reported by Patrassi,[2] Goldhamer and Barney,[3] Riehl [4] and Parade and Voegt.[5] Zimmerman and Curtis [6] reported a case of aleukemic myelosis with cutaneous nodules. In view of the low incidence of leukemic infiltrations in the skin in myeloid leukemia the following case was considered worthy of record.

REPORT OF A CASE

History.—P. K., a white man aged 44, was first seen on Dec. 29, 1939. The patient was in fairly good health until the first week of December 1939, at which time he noticed a swelling of the upper lip. The swelling increased progressively to the extent that it interfered with eating and talking. A few days later, the left testicle was noted to be larger than the right. After this, both

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1. Hollander, L.; Kastlin, G. J.; Perman, H. H., and Schmitt, C. L.: Myeloid Leukemia with Cutaneous Manifestations, Arch. Dermat. & Syph. **29**:821 (June) 1934.

2. Patrassi, G.: Ueber einen Fall von Übergang chronischer Myelose in Myeloglastenleukämie mit gleichzeitigem Auftreten leukämischer Hautgeschwülste, Folia haemat. **50**:415, 1933.

3. Goldhamer, S. M., and Barney, B. F.: Myelogenous Leukemia with Cutaneous Involvement, J. A. M. A. **107**:1041 (Sept. 26) 1936.

4. Riehl, G., Jr.: Chronische leukämische Myelose mit eigenartigan spezifischen Hauterscheinungen, Arch. f. Dermat. u. Syph. **177**:222, 1937.

5. Parade, G. W., and Voegt, H.: Zur Frage der Hautleukämie, Deutsches Arch. f. klin. Med. **185**:265 (Oct.) 1939.

6. Zimmerman, E. F., and Curtis, H. C.: Aleukemic Myelosis with Cutaneous Nodules, Arch. Dermat. & Syph. **33**:684 (April) 1936.

testicles increased considerably in size, although no pain was complained of. During the second week of December, the patient first became aware of numerous elevated reddened nodules of varying size, distributed over the face, back, chest, arms and legs. An extensive ulceration of the palate also developed. In spite of the loss of 15 pounds (6.8 Kg.) in weight and an increasing degree of weakness, the patient was able to continue his work as a machine operator until December 20. The past history and family history were essentially irrelevant. He had been married for eighteen years and had seven children.

Examination.—There were several indurated, elevated nodules scattered over the scalp. The upper eyelids were edematous, with a decided reduction of the palpebral fissure. The swollen upper lip projected out over the upper teeth, and the swelling extended upward, involving the nose and maxillary regions. A large ulcerating gangrenous lesion covered most of the hard palate and extended onto the soft tissues. Bilaterally there were numerous enlarged glands in the submandibular area. These enlargements were firm, nodular, discrete and painless and varied in size from that of a pea to that of a walnut. The heart and the lungs were normal. The spleen was palpable 3 fingerbreadths below the left costal margin. The edge of the liver was palpable. Glands similar to those in the submandibular area were also palpable in the axillary, inguinal and posterior and anterior cervical regions. There were numerous red to pink lesions distributed over the scalp, face, neck, trunk, arms and thighs. These lesions were indurated, elevated and freely movable and varied in diameter from 1 to 2 cm. They were most numerous on the back and chest. None of the nodules were ulcerated or crusted. The nature of the lesions and the swelling of the face are illustrated in figure 1 *A*.

Both testicles were enlarged, hard and painless on pressure and failed to transilluminate. The right epididymis was palpable as a hardened nodular cord. The prostate was moderate in size and normal in consistency.

Examination of the blood on December 29 showed 13 Gm. of hemoglobin per hundred cubic centimeters, 3,910,000 erythrocytes and 80,750 leukocytes, with a differential blood cell count of 3 per cent myelocytes, 7 per cent metamyelocytes, 15 per cent stab forms, 69 per cent polymorphonuclear neutrophils, 5 per cent lymphocytes and 1 per cent monocytes.

Aspiration of the sternal bone marrow revealed a myeloid hyperplasia with a suppression of the erythropoietic and megakaryopoietic elements. These findings were reflected in the peripheral blood by virtue of the leukocytosis, anemia and thrombopenia. Smears of the bone marrow showed a few myeloblasts, many myelocytes and a considerable number of polymorphonuclear cells.

In order to carry out additional studies the patient was admitted to the Research and Educational Hospital, University of Illinois, on Jan. 5, 1940. The urine showed no albumin, sugar or Bence Jones protein. The Wassermann and Kahn reactions of the blood were negative. Chemical examination of the blood showed 44 mg. of nonprotein nitrogen, 4.8 mg. of uric acid (gradually increased to 10 mg.), 86 mg. of sugar and 8.04 Gm. of total protein which decreased to 3.92 Gm., per hundred cubic centimeters. A roentgenogram of the chest showed an increase of hilar shadows and linear markings but no definite glandular enlargement. Roentgenograms of the long bones, pelvis and skull failed to demonstrate the presence of bony involvement.

Clinical Course.—When the patient entered the hospital his temperature was normal, pulse rate 100, respiratory rate 20 and weight 173 pounds (78.5 Kg.). He

Fig. 1.—A patient with chronic myeloid leukemia, showing *(A)* cutaneous nodules and edema of the face and neck and *(B)* improvement following two roentgen ray treatments. Note the purpuric areas in the clavicular region.

was up and about the ward, although he complained of some weakness and loss of appetite. The swelling of the lip, face and neck increased greatly. On January 12 he received a roentgen treatment of 25 r to the right side of the neck. The following day the temperature rose to 103 F., and it continued at a somewhat lower level, 100 to 101 F. Three days later the second and last roentgen treatment, 100 r, was

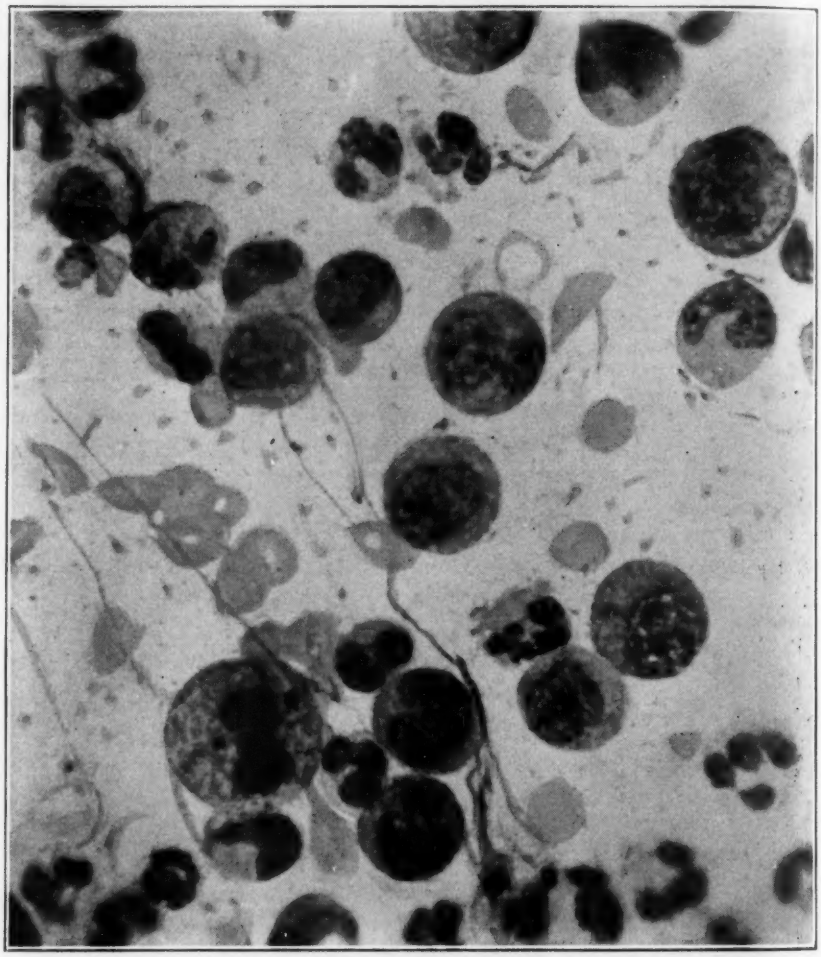

Fig. 2.—Photomicrograph of the sternal bone marrow. Note the myelocyte-metamyelocytic pattern and the absence of blast cells.

applied to the left axilla. It was noted at this time that the cutaneous lesions and edema of the face decreased greatly in intensity (fig. 1 *B*).

During this time he had intermittent attacks of epistaxis and lost considerable blood from the ulcer of the palate. Repeated studies of the blood (table) showed an increasing degree of anemia and a fluctuating leukocyte count with an increasing number of blast cells and young myeloid elements. This change in the peripheral

Results of Repeated Studies of the Blood of a Patient with Chronic Myeloid Leukemia

Date	Hemoglobin, Gm. per 100 Cc.	Erythrocytes, in Millions	Leukocytes	Hematocrit	Hematocrit (W. B. C.)	Mean Corp. Volume, Cu. Microns	Mean Corp. Hb., Micromicrograms	Mean Corp. Hb. Conc., per Cent	Sedimentation Rate, Mm. per Hr.	Corrected Rate, Mm. per Hr.	Differential Blood Smear: Myeloblasts	Myelocytes	Metamyelocytes	Stab Forms	Polymorphonuclear Neutrophils	Eosinophils	Basophils	Lymphocytes	Monocytes	Normoblasts	Reticulocytes, per Cent	Icterus Index, in Units	Platelets
12/29/39	13	3.91	80,750	38	4.5	97	33	34	45	28	0	3	7	15	69	0	0	5	1	2	1.3	7.5	.....
1/ 6/40	12	4.10	130,000	35	7.0	85	29	34	30	13	3	7	9	16	57	2	1	2	3	2	1.5	5	Reduced
1/12/40	25 roentgen rays																						
1/13/40	.....	.....	105,000	.....	.....	....	....	....	....	....	14	18	13	12	40	1	0	1	1	....	.....	.....	.....
1/15/40	.....	.....	58,500	.....	.....	....	....	....	....	....	....	....	....	....	....	...	...	...	...	....	.....	.....	.....
1/16/40	100 roentgen rays																						
1/16/40	.....	.....	60,000	.....	.....	....	....	....	....	....	5	1	8	20	65	0	0	0	0	....	.....	.....	.....
1/17/40	8.2	2.56	59,450	21.5	2.5	84	32	38	65	12	3	4	10	14	65	2	0	1	1	3	0.8	5	Reduced
1/18/40	.....	.....	65,000	.....	.....	....	....	....	....	....	7	3	8	20	60	0	0	0	0	....	.....	.....	.....
1/20/40	.....	.....	40,000	.....	.....	....	....	....	....	....	34	8	11	2	43	0	0	0	0	....	.....	.....	.....
1/22/40	.....	.....	125,000	.....	.....	....	....	....	....	....	36	8	17	5	30	2	0	0	2	12	.....	.....	.....
1/23/40	Blood transfusion (500 cc.)																						
1/23/40	7.5	2.31	100,000	22	5.0	95	32	34	48	6	44	5	14	8	21	1	2	2	1	7	3.0	10	.....
1/27/40	.....	.....	55,000	.....	.....	....	....	....	....	....	78	1	10	1	8	1	0	1	0	12	.....	.....	.....
1/28/40	7.5	2.60	60,000	24	2.5	92	29	31	59	15	80	0	2	1	12	1	1	3	0	7	0.8	10	5,000

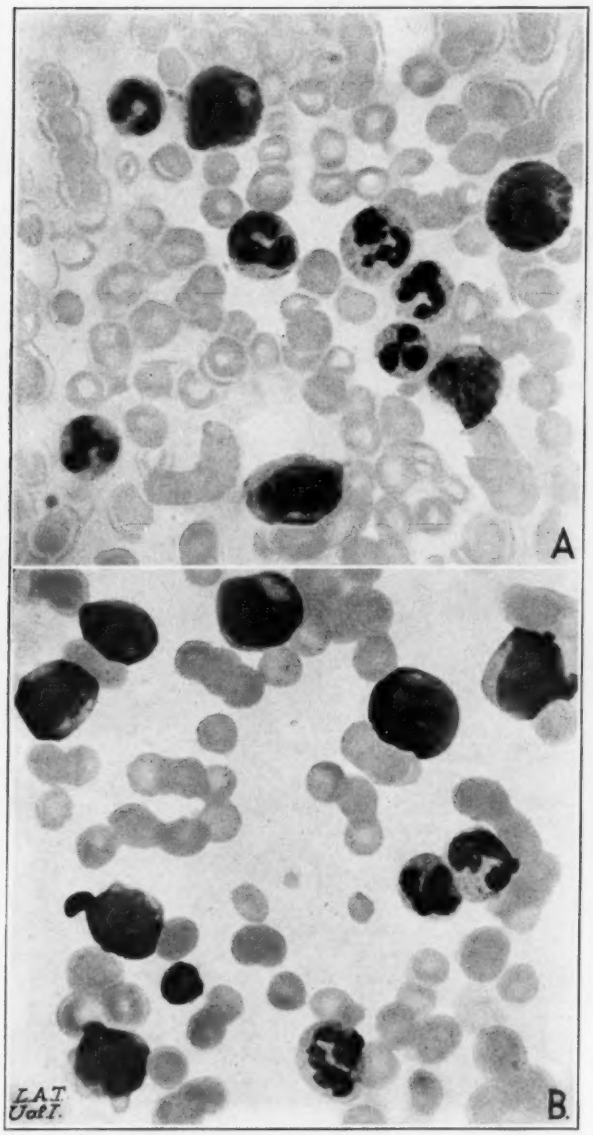

Fig. 3.—Photomicrographs of peripheral blood smears *(A)* when first examined (note the myelocytic neutrophilic pattern) and *(B)* in the terminal phase, showing "hiatus leukemicus."

blood picture from one of chronic myeloid leukemia to that of an acute myeloblastic phase is depicted in figure 3.

Because of the progressive anemia a blood transfusion was given on January 23. A few days prior to death widespread subcutaneous ecchymoses and generalized petechiae developed. He lapsed into a semicomatous state and died on January 29.

Biopsy.—On January 9 a specimen of skin was taken from one of the nodules on the anterior aspect of the right thigh. Sections were stained with hematoxylin and eosin and with Giemsa stain and May-Grünwald solution.

The epidermis showed no definite changes, and the papillary layer was practically free of infiltration. There was a diffuse cellular infiltration of the corium and subcutaneous tissue. The infiltration was most extensive in the subcutaneous

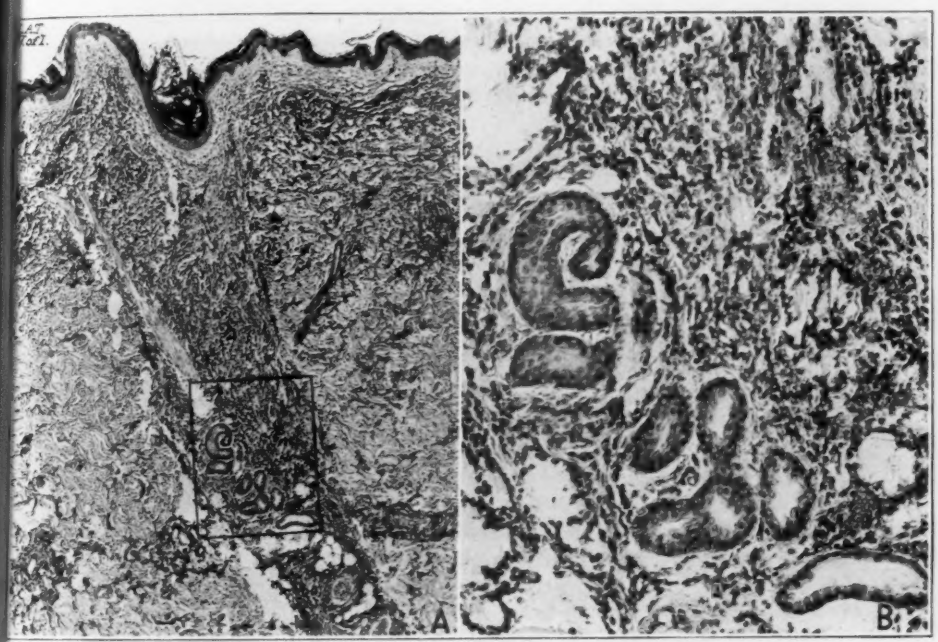

Fig. 4.—Photomicrographs of a section from a cutaneous nodule. *A*, low magnification, showing infiltration of leukemic cells in the corium and subcutaneous tissue, particularly about the sweat glands, blood vessels and hair follicles. *B*, high magnification of the area demarcated in *A*.

tissue, and the cells formed dense confluent masses about the sweat glands, adipose tissue, blood vessels and hair follicles. The reticulum about these infiltrations was increased and active in the formation of leukemic cells. The predominant cells were blast forms with occasional neutrophilic myelocytes. They were large, roughly rounded, mononucleated cells. The nuclei were large, with frequent irregular forms. Mitotic figures were not common. Neutrophilic leukocytes, metamyelocytes and phagocytic cells were occasionally encountered.

Autopsy (*Dr. W. O. Brown*).—The spleen weighed 1,760 Gm. and was symmetrically enlarged, with a purplish gray surface. There were several small infarcts,

averaging approximately 1 cm. in diameter, which were sharply demarcated from the surrounding pulp. The organ was firmer than normal, and the cut surface bulged slightly. On microscopic examination the typical picture of myelogenous leukemia was seen, with destruction of the normal architecture and dense infiltration of the pulp with all types of myelogenous cells. The majority of them were large round cells, measuring 25 to 30 microns in diameter, and appeared to be blast forms. The nuclei were round to vesicular with prominent nucleoli. Mitotic figures and degenerative forms were numerous. In addition to these there were numerous polymorphonuclear cells and scattered small erythropoietic islands composed of a few erythroblasts and nucleated red cells.

The liver weighed 2,280 Gm. It had a smooth, light purplish brown surface and was firmer than normal in consistency. The cut surface bulged slightly and was a uniform light brown with indistinct lobular markings. Microscopic sections showed an infiltration of the portal areas and the sinusoids by leukemic cells.

There was a discrete firm enlargement of the cervical, axillary, mesenteric and inguinal lymph nodes. The individual nodes measured up to 2 cm. in diameter, and masses of similar nodes up to 5 cm. in diameter partially surrounded the abdominal aorta. The mediastinum contained numerous discrete lymph nodes. In most instances the entire lymph node was destroyed and replaced by a dense homogeneous structure of leukemic cells. The degree of infiltration varied, and in some nodes a faint semblance of the original architecture was still visible. The cells resembled those described elsewhere.

The bone marrow was soft, mushy and deep gray on gross examination. There was degeneration of the bone marrow in excess of that expected from postmortem changes. Detailed studies were impossible, but the entire section appeared to be composed almost entirely of leukemic cells.

A section of the skin was taken from one of the small subcutaneous nodules. The epidermis was intact and appeared normal. The cutis showed infiltrations of leukemic cells about the blood vessels. There were numerous infiltrations of leukemic cells in the deeper layers of the cutis and about the sebaceous glands.

The right testicle weighed 145 Gm. and the left 120 Gm. The tunica albuginea measured up to 12 mm. in thickness and was pale gray. The testicles were much firmer than normal. A microscopic section showed the tunica albuginea thickened by a diffuse infiltration of leukemic cells, which were densely packed into the testicle, separating the seminiferous tubules.

The heart, lungs, kidneys, pancreas, trachea, prostate, submaxillary glands, adrenals and parathyroids showed a general infiltration of tissue by myelogenous cells of all types.

COMMENT

There are several points of interest in this case: (1) the disparity between the hematologic and hemohistologic observations and (2) the prognostic significance of cutaneous lesions in myeloid leukemia.

The peripheral blood in the early stage of this case was that of chronic myelogenous leukemia in the polymorphonuclear neutrophilic phase. The bone marrow was predominantly a myelocytic, neutrophilic hyperplasia with a few typical myeloblasts. A simultaneous biopsy of the skin revealed many blast cells with frequently a number of early neutrophilic myelocytes. This would suggest a primary autochthonous cutaneous derivation of the leukemic blast cells from the local reticulo-

endothelial elements rather than infiltrations of leukemic cells of metastatic origin. This type of origin for the monocytes in the cutaneous manifestations of monocytic leukemia was observed by Montgomery and Watkins [7] and Freeman and Koletsky.[8] The implications are great that the rapid pouring of myeloblasts into the peripheral blood occurred mostly from the local cutaneous lesions rather than from the bone marrow or from the blood stream. The acute leukemic phase was apparently hastened by the roentgen ray treatments. The terminal blood picture was that of a "hiatus leukemicus," which is considered pathognomonic of acute myeloid leukemia.[9]

The appearance of leukemic nodules in the skin in the course of chronic myeloid leukemia is of grave prognostic import. Goldhamer and Barney,[3] who reviewed 16 previously reported cases of myeloid leukemia with cutaneous manifestations and reported 1 of their own, found the duration of life after the appearance of the cutaneous lesions to vary from eleven days to four months, the average being sixty-four days. In contrast to this short period of survival, Leavell [10] reported 87 cases of chronic myeloid leukemia without specific manifestations of the skin in which the average duration of life after the onset of symptoms was three and two-tenths years. In 9 patients with chronic lymphatic leukemia and specific cutaneous lesions the duration of life after the onset of symptoms was three and five-tenths years.

SUMMARY AND CONCLUSIONS

A case of chronic myeloid leukemia with specific cutaneous manifestations is reported.

The autochthonous cutaneous nodules in chronic myeloid leukemia may serve as a source of rapid myeloblastic proliferation, and their presence is probably the main factor in bringing about the rapidly acute phase of the disease.

The appearance of cutaneous manifestations during the course of chronic myeloid leukemia denotes an impending rapid terminal phase.

1853 West Polk Street.

3211 West Madison Street.

7. Montgomery, H., and Watkins, C. H.: Monocytic Leukemia: Cutaneous Manifestations of the Naegeli and Schilling Types; Hemocytologic Differentiation, Arch. Int. Med. **60**:51 (July) 1937.

8. Freeman, H. E., and Koletsky, S.: Cutaneous Lesions in Monocytic Leukemia: Report of Two Cases, with Pathologic Study, Arch. Dermat. & Syph. **40**:218 (Aug.) 1939.

9. Naegeli, O.: Blutkrankheiten und Blutdiagnostik, ed. 5, Berlin, Julius Springer, 1931.

10. Leavell, B. S.: Chronic Leukemia: A Study of the Incidence and Factors Influencing the Duration of Life, Am. J. M. Sc. **196**:329 (Sept.) 1938.

PAPULAR URTICARIA PIGMENTOSA

REPORT OF A CASE

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HANS J. SCHWARTZ, M.D.

AND

N. CHANDLER FOOT, M.D.

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Accepted classifications of urticaria pigmentosa do not include a purely papular form. The outstanding monographs on the subject and the standard dermatologic textbooks recognize three distinct clinical types: macular, nodular and maculonodular. In the majority of cases the condition is macular, and the purely nodular type occurs in only a small percentage of the total number. Finnerud,[1] in an admirable study of 152 cases of this dermatosis, the most recent and complete summary, reported that in 61.7 per cent of the cases the condition was macular, in 30.5 per cent maculonodular and in 7.8 per cent nodular.

We wish to report the following case of papular urticaria pigmentosa because this form of the dermatosis is extremely rare.

REPORT OF CASE

G. P., a white man aged 32, was admitted to the dermatologic clinic of the New York Hospital on Dec. 28, 1938. He presented an eruption which he had had since the age of 1 year and which involved the entire cutaneous surface with the exception of that of the face. The patient stated that there had been no change in the appearance, distribution or configuration of the eruption within his memory. There had been no subjective symptoms except occasional pruritus associated with the appearance of wheals.

Examination of the skin revealed confluent, violaceous and yellowish brown moderately indurated papules, varying in diameter from 1 to 3 mm. and elevated from a fraction to 1 mm., covering the entire body with the exception of the face (fig. 1). On the trunk and in the axillas the lesions were more numerous than on the extremities. In the axillas and around the umbilicus the lesions were chamois colored and slightly resembled xanthoma. Many of the papules were follicular. On the extremities the lesions were less elevated and definitely follicular. There was no change in these lesions during the time we observed the patient, two years. We were unable to make a clinical diagnosis of this eruption. The hands

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From the Dermatological Clinic of the New York Hospital and the Department of Medicine of Cornell University Medical College.

1. Finnerud, C. W.: Urticaria Pigmentosa (Nodular Type), Arch. Dermat. & Syph. **8**:344 (Sept.) 1923.

and feet presented the typical picture of erythema pernio. They were purplish, cool to the touch and moistened with sweat. A number of the times that we examined the patient the purplish mottling and reticulation of cutis marmorata were present on the extremities. There was marked dermographism, the slightest trauma eliciting a welt with a large halo of bright erythema.

A general physical examination showed no other essential abnormalities, and it was concluded that the patient had a psychoneurosis. He complained that for the previous fourteen years he had been depressed and unable to concentrate. He

Fig. 1.—Left side of chest and axilla, showing the numerous confluent papules with no areas of clear skin.

stated that for the last three months he had had daily severe night sweats, had lost 14 pounds (6.4 Kg.) and had been chronically fatigued. Perivascular examination revealed a definite Buerger sign. Oscillometric readings were normal. The patient was reported to show a pronounced vasomotor unbalance.

Roentgenograms of the lungs showed no evidence of tuberculosis. The basal metabolic rate was + 4 per cent. The Wassermann reaction of the blood was negative. The results of urinalysis were negative. The cholesterol content of the blood was 194 mg. per hundred cubic centimeters of blood; the sugar content, 100 mg., and the phosphorus content (serum), 2.7 mg. Roentgenologic examination

of the skull and of the bones of the upper extremities, chest, pelvis and lower extremities failed to show any evidence of xanthomatous or other destructive lesions.

Microscopic sections (fig. 2) showed that the stratum corneum was not much changed, but here and there it exhibited superficial funnel-shaped depressions filled with horny material. The stratum spinosum was thin, and the basal layer showed definitely increased and generalized pigmentation. The rete pegs were almost completely lacking under the lesion but reappeared at its margins. The most striking feature was the presence of numerous closely packed granular cells in the upper layers of the much thickened corium.

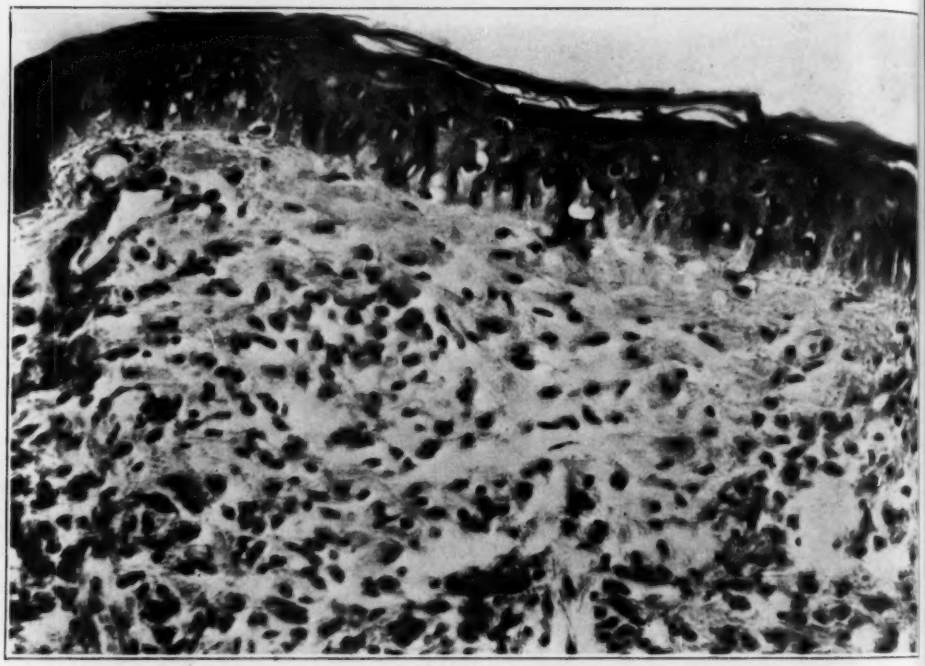

Fig. 2.—Photomicrograph of a lesion (× 350). Note the flattened atrophic epidermis and the closely packed mast cells in the underlying corium. The pigment of the basal cell layer does not show well in this photomicrograph.

The sections stained with hematoxylin and eosin showed pyknotic nuclei and slightly granular cytoplasm and might have passed unnoticed, but in the sections treated with Masson stain the granular characteristics were so marked as to attract attention immediately. The cells showed decided affinity for the ponceau in the stain and were seen to be polygonal with solid nuclei and brick red granular cytoplasm.

With nile blue sulfate and Giemsa's method some of the cells stained a dark navy blue or azure and were identified as mast cells. Their distribution was widespread and disorderly and not definitely perivascular. They apparently lay in the spaces in the tissue and in the lymphatics of the corium. These cells formed an almost solid zone between the epidermis and the deeper layers of the corium,

which were considerably frayed out and rather poor in elastic fibers. Other inflammatory cells, such as lymphocytes, monocytes, plasma cells and eosinophils, were conspicuously absent from the picture. The vessels of the corium were not particularly congested with blood. The lesion was undoubtedly that of urticaria pigmentosa.

COMMENT

A survey of the literature has revealed 2 cases (in the foreign literature) which are similar to the case we have described.

Pautrier and Fernet [2] reported a case of this condition of four years' duration in a man aged 23. They described the eruption as consisting of small slightly elevated papules, some violaceous, some yellowish brown and others presenting only a slightly brownish pigmentation. The papules were in such close proximity that practically no normal skin was visible. The entire cutaneous surface with the exception of that of the face and hands was involved. Friction resulted in edema and erythema of the individual papules. There was also pronounced dermographism. Microscopic examination of tissue from a papule showed the typical picture of urticaria pigmentosa with pigmentation in the basal cell layer of the epidermis and mast cells in the corium.

Richter [3] described a case of "urticaria pigmentosa naeviformis" which was apparently almost identical with the case we have reported (fig. 3). A white boy aged 16 presented a generalized eruption which had been present since the age of 1 year. He had had no subjective symptoms except from superimposed attacks of acute urticaria, and he stated that there had at no time been any change in the eruption. He presented confluent papules, 2 to 3 mm. in diameter and 0.5 to 1 mm. high, which were erythematous, violaceous and yellowish brown and involved the entire body with the exception of the face. In the axillas and back of the knees the papules were more pronounced and the skin appeared leathery. There was a decided dermographism. Microscopic examination showed the characteristic picture of urticaria pigmentosa with pigmentation in the basal cell layer of the epidermis and a profusion of mast cells in the corium.

E. Scolari [4] described a case of urticaria pigmentosa lichenoides which had some of the features of our case but which presented numerous differences. The patient was a child aged 9 years with an eruption of sixteen months' duration distributed over the entire cutaneous surface with the exception of that of the hands and feet. At the onset

2. Pautrier, L. M., and Fernet, P.: Cas d'urticaire pigmentaire à début tardif, Bull. Soc. franç. de dermat. et syph. **20**:107, 1909.

3. Richter, W.: Ueber einen Fall von Urticaria pigmentosa naeviformis, Arch. f. Dermat. u. Syph. **162**:771, 1931.

4. Scolari, E.: Urticaria pigmentosa lichenoide, Gior. ital. di dermat. e sif. **75**:1207 (June) 1934.

erythematous patches appeared accompanied by fever, which was followed by edema in the erythematous patches. The eruption on the face and legs retrogressed entirely in a few days, but in other parts the elements

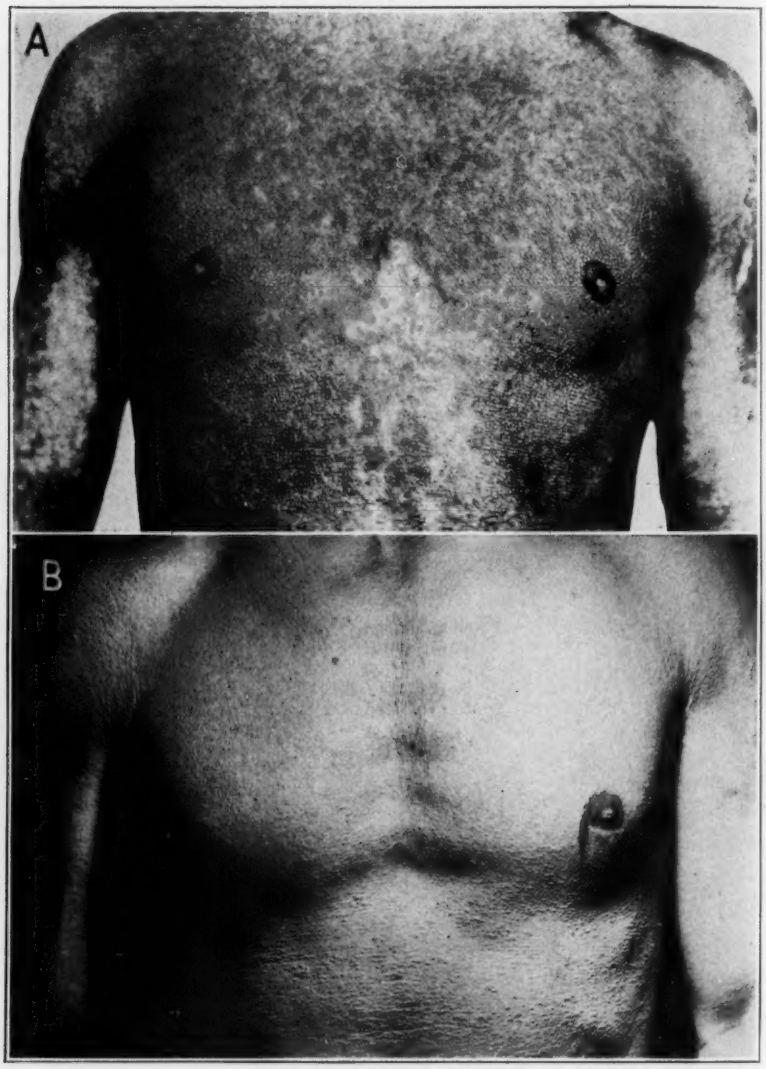

Fig. 3.—*A*, Richter's patient.[3] Note the similarity to the eruption in our case (*B*).

instead of becoming leveled assumed the appearance of papules. Examination showed a miliary papular eruption with hemispherical, circular and polygonal, red or brownish red, hard, densely distributed lesions.

The intrapapular skin was pigmented. There were present also some miliary pustules. A second urticarial outbreak consisted of an edematous elevation limited to the preexisting papules and was not associated with the formation of new papules. A microscopic section showed mastocytic tumors of the type of Unna.

SUMMARY

A case of papular urticaria pigmentosa of thirty-one years' duration in a man aged 32 is reported. Only 2 similar cases, reported by Pautrier and Fernet and by Richter, have been found in a survey of the literature. A third case, that of Scolari, presented some of the features of our case but differed in a great many respects. These cases, which we have abstracted, were reported in foreign journals.

The clinical appearance of the eruption does not suggest any of the generally recognized forms of this dermatosis, and the diagnosis was made by a microscopic study of some of the lesions. In retrospect, the lesions in the axillas and around the umbilicus presented the xanthomatous appearance which has been noted in some cases of urticaria pigmentosa, particularly the nodular type.

The lesions were confluent and involved the entire cutaneous surface except that of the face. They varied in diameter from 1 to 3 mm. and were elevated from a fraction to 1 mm. They were violaceous and yellowish brown, except in the axillas and around the umbilicus, where they were chamois colored. There was marked dermographism. There was no change in the appearance or configuration of the lesions during our two year period of observation, nor had the patient noted any variation within his memory. This feature was emphasized by Richter in describing the condition in his case as neviform.

Microscopic study of sections of a lesion in our case showed the typical picture of urticaria pigmentosa, including increased generalized pigmentation in the basal cell layer and numerous mast cells in the corium. These observations correspond closely to the description by Pautrier and Fernet and by Richter.

The patient also had typical erythema pernio and cutis marmorata. Perivascular examination revealed a decided vasomotor unbalance.

118 East Sixty-First Street.

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HISTOPLASMOSIS WITH MUCOCUTANEOUS MANIFESTATIONS

REPORT OF A CASE

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ARTHUR L. AMOLSCH, M.D.
AND
LOREN W. SHAFFER, M.D.
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In recent years there has been an unprecedented number of cases of histoplasmosis reported. What has heretofore been regarded as a rare semitropical disease is being found in increasing numbers of cases throughout the United States, the total now having reached about 35 cases. Meleney [1] reviewed 32 cases occurring up to July 1940. Since that time 1 case has been reported from the Mayo Clinic [2] and 1 patient has been under observation at the University of Michigan. The latter patient died just prior to the death of our patient. The relatively high incidence (7 cases) in the state of Michigan is particularly interesting. The purpose of this report is to add another case to the growing list and also to point out a previously unrecorded manifestation. The close resemblance of systemic histoplasmosis to American leishmaniasis has been pointed out frequently.[1] The patient described here exhibited a mucocutaneous form of histoplasmosis which simulated closely the mucocutaneous type of American leishmaniasis.

REPORT OF CASE

A 45 year old Polish man, who has resided in Michigan continuously for sixteen years, was admitted to the City of Detroit Receiving Hospital on Oct. 28, 1940, complaining of severe hoarseness, severe pain in the throat and pain on swallowing since March 1940. He also complained of weakness and loss of 35 pounds (16 Kg.) in weight since July 1940. In July 1940 an ulcer developed on the left side of the upper lip along with a progressive cough productive of large amounts of foul sputum. In the week prior to admission he had noticed simular ulcerations on the penis and about the anus.

From the Department of Dermatology and Syphilology and of Pathology, Wayne University College of Medicine, and from the City of Detroit Receiving Hospital.

1. Meleney, H. E.: Histoplasmosis: A Review, Am. J. Trop. Med. **20**: 603, 1940.

2. Brown, A. E.; Havens, F. Z., and Magath, T. B.: Histoplasmosis: Report of Case, Proc. Staff Meet., Mayo Clin. **15**:812, 1940.

On examination the patient appeared chronically ill. He was emaciated and weak and had an irregular intermittent fever with a temperature up to 100 and 101 F. He presented a deeply punched-out destructive ulceration covered with a dense crust involving the left half of the upper lip, with no induration or noticeable inflammatory reaction. There were numerous superficial ulcerations of the mucous membrane of the mouth, especially on the tongue and palate. Indirect laryngoscopic examination revealed involvement of the hypopharynx, larynx and vocal cords by superficial ulcerations and granulation tissue. The patient's skin was sallow and pallid. On the prepuce and about the anus were several deep punched-out ulcers covered with a purulent discharge. No enlargement of the lymph glands was noted, and, although the spleen was questionably palpable, the liver was not. The blood pressure was 95 systolic and 55 diastolic.

Cancer was not considered in the differential diagnosis because of the distribution and lack of induration of the lesions. Syphilis was thought improbable

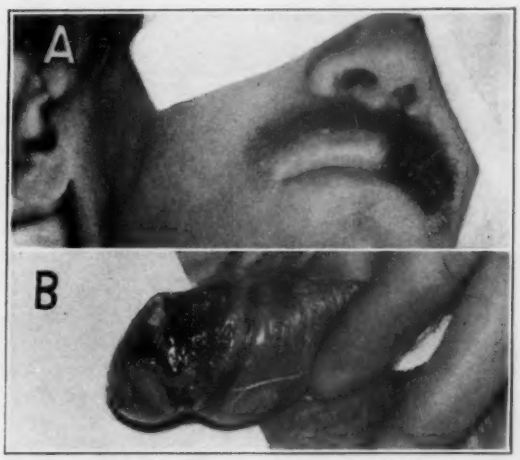

Fig. 1.—Deeply punched-out ulcers in a case of histoplasmosis. *A*, heavily crusted ulcer of the upper lip. *B*, extensive ulcers of the prepuce and glans penis.

in spite of a coincidental positive serologic reaction because the patient's private physician had been giving him continuous treatment since March with overlapping, alternating courses of arsenic and bismuth. Dark field examinations of the lesions showed no spirochetes. Noma was considered, but smears were negative. Tuberculosis was ruled out because examinations of the sputum showed no organisms and the pulmonary fields were clear in the roentgenograms. However, a large aneurysm of the ascending aorta was found to be present, extending 10 cm. to the left of the midline and having calcified walls.

Repeated urinalyses showed a 1 to 4 plus reaction for albumin, with occasional red and white cells. The value for hemoglobin varied from 10 to 6 Gm. A study of the red blood cells showed a normochromic, microcytic anemia. The leukocyte count was never over 4,000 and on several occasions dropped to 1,650. The cells showed evidence of a severe toxemia with a degenerative left shift. There was a thrombopenia, with 74,000 platelets. The reticulocyte count was 2.1 per cent. Both the Kline and the Kahn serologic reactions were strongly positive.

Histologic examination of tissue from lesions on the lip and in the perianal region showed a chronic granuloma containing innumerable organisms simulating Leishmaniae. On further morphologic and cultural studies the organism was proved to be Histoplasma capsulatum. In view of this observation, daily blood smears from the patient were studied and a sternal puncture was made once in unsuccessful attempts to find the organism. Fresh material was inoculated into mice, and the organism was recovered from a small necrotic area in the liver of

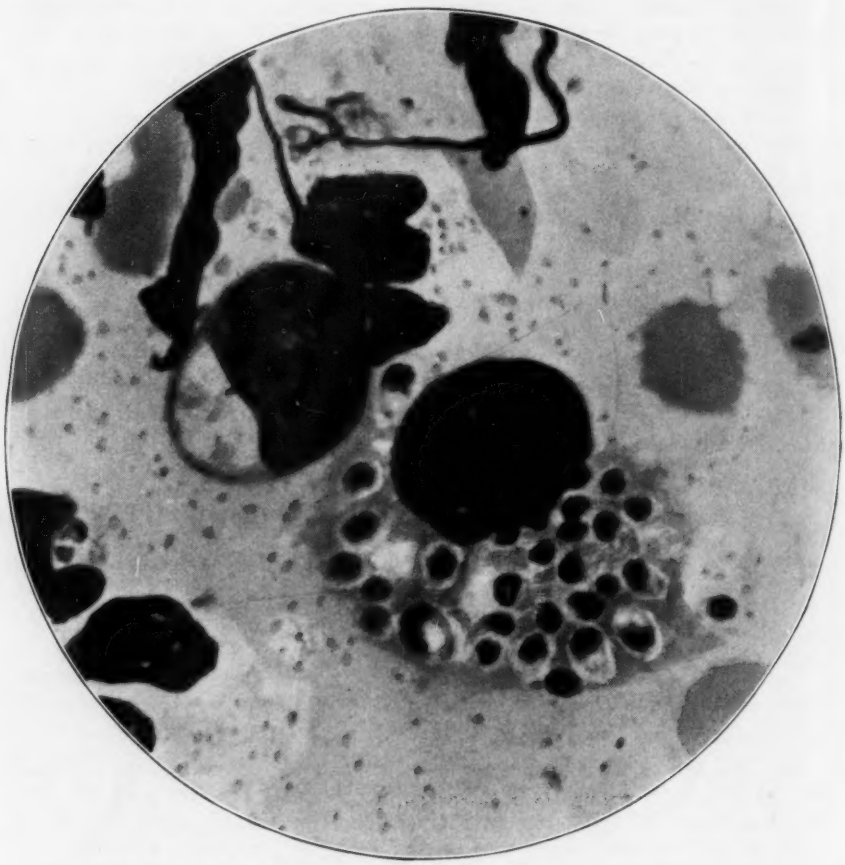

Fig. 2.—Histoplasma capsulatum phagocytosed in a macrophage (smear from a biopsy specimen of an anal ulcer; Leishman's stain; × 1,400).

one of the animals after about two months. A culture of Histoplasma recovered from the mouse was inoculated intraperitoneally into a 4 week old puppy. The animal died from the infection in forty-five days and exhibited massive involvement of the liver, spleen and peritoneum resembling tuberculosis.

The patient was treated both locally and systemically. Potassium permanganate soaks, gentian violet, 2 per cent thymol in olive oil and sulfanilamide dusting powder all kept the lesions free from secondary infection but had no healing effect on the ulcers. Intravenous administration of fluids, high vitamin

dosage, especially of the B complex, and several transfusions gave no lasting response. Then stibium chloride (neostam) was given but was tolerated poorly. The patient finally refused the antimony entirely after the first injection of a second course of four injections. Sixty grains (4 Gm.) of sulfathiazole (2-[para-aminobenzenesulfonamido]-thiazole) was administered daily with no improvement in the ulcers or in the general condition. The patient claimed the drug made him feel so much worse that its administration was discontinued after ten days.

Despite all therapy, progression was steadily downhill, and terminal purpuric macules developed on the legs. He died on Feb. 2, 1941.

The postmortem examination was made twelve hours after death. The essential features other than the cutaneous lesions and the aortic aneurysm were the changes in the larynx, spleen and adrenal glands. The entire larynx, including the vocal cords, was extensively involved by several deep granulomatous ulcers. The spleen was enlarged to 590 Gm. but was not unusual in its gross appearance. Both adrenal glands were decidedly enlarged, measuring 7 cm. in length, 3.5 cm. in width and 1 cm. in thickness. They were rubbery in consistency and on section revealed numerous caseous-appearing areas almost entirely replacing the glandular tissue. In the mucosa of the small bowel, in the region of the jejunum and the first part of the ileum, there were four minute white plaques from 1 to 2 mm. in diameter. No intestinal ulcerations were found. The lungs showed a terminal pneumonia and congestion. The liver showed only a chronic passive congestion. Bilateral pyelonephritis was present.

Despite the presence of innumerable organisms in the material taken for biopsy and positive cultures both on artificial mediums and from inoculated mice, no organisms whatever could be seen in the sections taken at autopsy or in direct smears. Cultures on suitable mediums from the postmortem material showed no growth of fungus during four weeks of observation.

Microscopic examination of the laryngeal tissue showed a chronic granuloma with no demonstrable organisms. There were widening and congestion of the sinuses of the spleen. The adrenal tissue showed the caseous replacement with the formation of many tubercles or pseudotubercles. Whether these were actually tuberculous or due to Histoplasma could not be demonstrated. No tubercle bacilli could be found with special stains.

COMMENT

Many unusual features were present in this case, not the least of which was the mucocutaneous involvement so strongly resembling mucocutaneous leishmaniasis. No other case of histoplasmosis has been reported in the literature in which this manifestation was present. In this case there were no miliary pseudotubercles in the lungs, an observation so commonly reported in histoplasmosis. Intestinal ulcerations were also lacking, despite the extensive oral and anal involvement. However, the caseous destruction of the adrenal glands by a process strongly resembling tuberculosis was present. The presence of innumerable organisms in the biopsy specimens and none in the autopsy material gives rise to speculation. Whether this was due to the twelve hour interval between death and the examination or to the effect of the medication cannot be stated definitely. A purely speculative premise supposes that either the antimony or the sulfathiazole killed the organisms

and the patient died of adrenal insufficiency. Unfortunately, this aspect was not considered before the patient's death and substitution therapy was not instituted. The presence of the large syphilitic aneurysm further complicated the patient's chances of recovery. It is interesting that in this case the disease did not appear to be primarily of the reticuloendothelial system, a contradiction of a statement which is repeated throughout the literature.

SUMMARY

An unusual case of histoplasmosis has been reported, in which there was a manifestation heretofore not recorded, namely, mucocutaneous involvement closely resembling mucocutaneous (American) leishmaniasis.

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NUTRITIONAL DERMATOSES IN THE RAT
VI. THE EFFECT OF PANTOTHENIC ACID DEFICIENCY

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Signs of deficiency, including cutaneous alterations, occur in rats and chicks which are fed purified diets low in the vitamin B complex and supplemented with the synthetic forms of thiamine, riboflavin, nicotinic acid and pyridoxine (vitamin B_6). If whole liver or yeast is substituted for the four vitamins there are no signs of deficiency. Therefore there are additional members of the vitamin B complex in the natural foodstuffs. One of these has been identified as pantothenic acid.

Fractionation of "water-soluble vitamin B" was originally accomplished by autoclaving whole yeast.[1] By this procedure the antineuritic fraction, vitamin B_1 (thiamine), was destroyed, but the growth-promoting, "antidermatitic," heat-stable fraction, vitamin B_2 (vitamin G), was unaffected. Later other methods of separation were introduced. Biologically active fractions were obtained in crude adsorbates, eluates and precipitates which were prepared from aqueous extracts of foods rich in the complex. Treatment of whole liver or yeast extracts with impure aluminum silicate (fullers' earth) removed thiamine, riboflavin and pyridoxine by adsorption. The nonadsorbable portion, i. e. the filtrate, contained additional active factors. One of these, the so-called "filtrate factor," was identified as pantothenic acid.[2] Other substances reported to exist in such filtrate preparations are: a factor which complements the

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1. Smith, M. I., and Hendrick, E. G.: Nutrition Experiments with Brewer's Yeast, with Especial Reference to Its Value in Supplementing Certain Deficiencies in Experimental Rations, Pub. Health Rep. **41**:201 (Feb. 5) 1926.

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antidermatitic activity of pyridoxine,[3] a factor which prevents "spectacle eye condition" in rats,[4] additional growth factors [5] and an anti-gray-hair factor other than pantothenic acid.[6] When the aluminum silicate adsorbate is treated with barium hydroxide or other suitable materials, the resulting eluate contains pyridoxine.[7] According to Oleson, Bird, Elvehjem and Hart,[8] the eluate also contains factors which prevent hemorrhage of the paws and a paralytic condition which may be the vitamin B_4 deficiency syndrome described by Reader.[9] According to György, Goldblatt, Miller and Fulton,[10] a factor which prevents panmyelophthisis is present in the eluate. By a different technic investigators at the University of Wisconsin separated a growth-promoting fraction, which they named factor W. It was precipitated from whole liver extract by alcohol and ether.[11] On the basis of solubility and lability to heat it was distinguished from other factors.[12] Although there is nicotinic acid in

3. (*a*) Schneider, H.; Steenbock, H., and Platz, B. R.: Essential Fatty Acids, Vitamin B_6 and Other Factors in the Cure of Rat Acrodynia, J. Biol. Chem. **132**:539 (Feb.) 1940. (*b*) Supplee, G. C.; Bender, R. C., and Kahlenberg, O. J.: The Effect of Complementing Factors on the Quantitative Response and Specificity of Vitamin B_6, J. Nutrition **20**:109 (Aug.) 1940.

4. Oleson, J. J.; Elvehjem, C. A., and Hart, E. B.: Spectacle Eye Condition in Rats, Proc. Soc. Exper. Biol. & Med. **43**:161 (Jan.) 1940.

5. (*a*) Woolley, D. W.: Observations on the Multiple Nature of the "Rat Filtrate Factor," Proc. Soc. Exper. Biol. & Med. **43**:352 (Feb.) 1940. (*b*) Mohammed, A. M.; Emerson, O. H.; Emerson, G. A., and Evans, H. M.: Properties of the Filtrate Factor of the Vitamin B_2 Complex with Evidence for Its Multiple Nature, J. Biol. Chem. **133**:17 (March) 1940. (*c*) Oleson, J. J., and Black, S.: Factor W and Pantothenic Acid in the Nutrition of the Rat, ibid. **133**:lxxiii (May) 1940. (*d*) Lythgoe, B. M.; Macrae, T. F.; Stanley, R. H.; Todd, A. R., and Work, C. E.: The Vitamin B Complex of Liver: The Identity of the Liver Filtrate Factor with Pantothenic Acid, Biochem. J. **34**:1337 (Nov.) 1940.

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7. György, P.: Investigations on the Vitamin B_2 Complex: The Differentiation of Lactoflavin and the "Rat Anti-Pellagra" Factor, Biochem. J. **29**: 741 (March) 1935.

8. Oleson, J. J.; Bird, H. R.; Elvehjem, C. A., and Hart, E. B.: Additional Nutritional Factors Required by the Rat, J. Biol. Chem. **127**:23 (Jan.) 1939.

9. Reader, V.: A Second Thermolabile Water Soluble Accessory Factor Necessary for the Nutrition of the Rat, Biochem. J. **23**:689, 1929.

10. György, P.; Goldblatt, H.; Miller, F. R., and Fulton, R. P.: Panmyelophthisis with Hemorrhagic Manifestations in Rats on a Nutritional Basis, J. Exper. Med. **66**:579 (Nov.) 1937.

11. Elvehjem, C. A.; Koehn, C. J., and Oleson, J. J.: A New Essential Dietary Factor, J. Biol. Chem. **115**: 707 (Oct.) 1936.

12. Black, S.; Frost, D. V., and Elvehjem, C. A.: The Relation of Vitamin B_6 and Pantothenic Acid to Factor W Studies, J. Biol. Chem. **132**:65 (Jan.) 1940.

crude preparations of liver and yeast which supply the unidentified components of the vitamin B complex, no indisputable evidence has established nicotinic acid as an essential vitamin for the rat.[13] Dann and Kohn [14] observed that with a diet low in nicotinic acid growing rats synthesized coenzyme at a rate which utilized more nicotinic acid than was ingested, showing that nicotinic acid was synthesized by the rats. Choline,[15] biotin,[16] inositol [17] and paraaminobenzoic acid [18] have been considered members of the vitamin B complex; it was shown that under certain experimental conditions each was necessary for the normal nutrition of the rat. The relation of these four substances to the unidentified biologically active factors has not been conclusively explained.[18a]

In this series there have appeared descriptions of nutritional dermatoses which resulted from deficiencies of pyridoxine,[19] of riboflavin,[20] of the entire complex other than thiamine [21] and of the entire complex other than thiamine and riboflavin.[22] The present report deals with the cutaneous alterations in rats fed thiamine, riboflavin, pyridoxine and nicotinic acid and deprived of pantothenic acid and other additional biologically active members of the vitamin B complex.

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13. (*a*) Macrae, T. F., and Edgar, C. E.: The Water Soluble B Vitamins: Nicotinamide and Other Pyridine Derivatives in the Nutrition of the Rat, Biochem. J. **31**: 2225, 1937. (*b*) Frost, D. V., and Elvehjem, C. A.: Further Studies on Factor W, J. Biol. Chem. **121**:255 (Oct.) 1937. (*c*) Chick, H.; Macrae, T. F.; Martin, A. J. P., and Martin, C. J.: Experiments with Pigs on Pellagra and Producing Diets, Biochem. J. **32**:844 (May) 1938.

14. Dann, W. J., and Kohn, H. I.: The Factor V (Coenzymes I and II) Content of Rat Tissues: Evidence of Synthesis of Nicotinic Acid by Rat, J. Biol. Chem. **136**:435 (Nov.) 1940.

15. György, P., and Goldblatt, H.: Choline as a Member of the Vitamin B Complex, J. Exper. Med. **72**:1 (July) 1940.

16. György, P., and Poling, C. E.: Further Experiments on Nutritional Achromotrichia in Rats and Mice, Proc. Soc. Exper. Biol. & Med. **45**:773 (Dec.) 1940. Woolley.[5a]

17. Pavcek, P. L., and Baum, H. M.: Inositol and Spectacle Eye Condition in Rats, Science **92**:502 (May 23) 1940.

18. Ansbacher, S.: Para-Amino-Benzoic Acid: A Vitamin, Science **93**:164 (Feb. 14) 1941.

18a. Vitamins for Gray Hair, J. A. M. A. **118**:302 (Jan. 24) 1942.

19. Sullivan, M., and Nicholls, J.: Nutritional Dermatoses in the Rat: I. Vitamin B_6 Deficiency, J. Invest. Dermat. **3**:317 (Aug.) 1940.

20. Sullivan, M., and Nicholls, J.: Nutritional Dermatoses in the Rat: IV. Riboflavin Deficiency, J. Invest. Dermat. **4**:181 (June) 1941.

21. Sullivan, M., and Nicholls, J.: Nutritional Dermatoses in the Rat: II. Skin Changes in Rats Deficient in the Entire Vitamin B Complex Other Than Thiamin, J. Invest. Dermat. **3**:337 (Aug.) 1940.

22. Sullivan, M., and Nicholls, J.: Nutritional Dermatoses in the Rat: III. Gangrene and Spontaneous Amputation of the Digits Produced by the Combined Deficiency of Vitamin B_6 and the Filtrate Components, J. Invest. Dermat. **4**:123 (April) 1941.

EXPERIMENTS

Experiment 1.—Forty-five rats each weighing from 35 to 45 Gm. and approximately 21 days of age were fed a basal diet of the following composition: acid-washed casein, 18 per cent; sucrose, 66 per cent; McCollum salts 51,[23] 6 per cent; washed butterfat, 8 per cent; and cod liver oil, 2 per cent. Five-tenths cubic centimeter of a solution containing 25 micrograms each of thiamine hydrochloride, riboflavin and pyridoxine and 15 micrograms of nicotinic acid was given to each rat daily except Sunday.[24] The basal diet was prepared every week, and the solution of synthetic vitamins was mixed three times a week. All food materials were stored in the refrigerator.

During the first three weeks the rats gained approximately 10 Gm. per week; they had good appetites and appeared lively. The quality of the fur and the

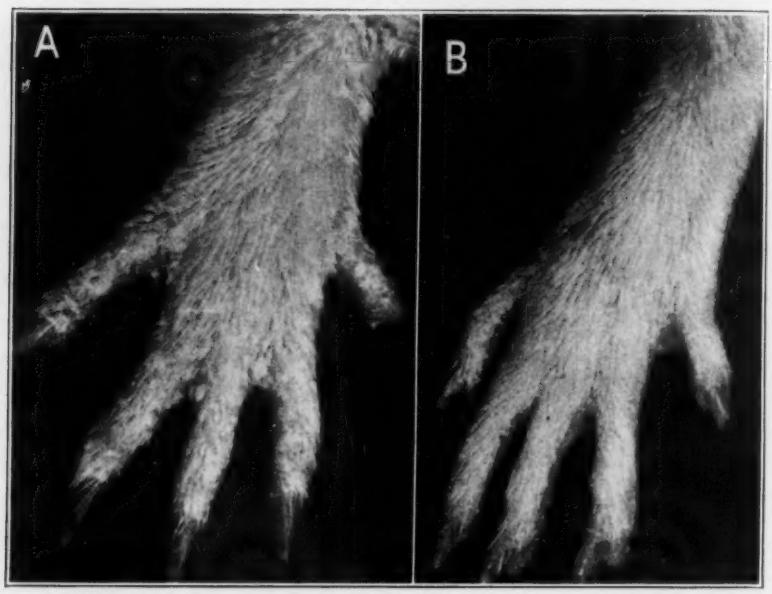

Fig. 1.—*A*, mild scaling of the paws due to deficiency of a filtrate component other than pantothenic acid. *B*, response to administration of crude liver filtrate preparations or corn oil. Pyridoxine failed to prevent or cure this scaliness.

texture of the skin was normal until the third or fourth week, when a fine dry scaling was observed in the flexure of each paw and leg (fig. 1*a*). There was a gradual extension of the scaling onto the dorsum of the paw until it involved the interphalangeal webs and to a less extent the plantae. Little or no erythema and no edema preceded or accompanied the scaling. At about the same time there was some scaling of the distal third of the tail.

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23. Adams, G., and McCollum, E. V.: A Method for the Biological Assay of Cod Liver Oil, J. Biol. Chem. **78**:495 (July) 1928.

24. In a group of 15 rats the supplements were incorporated in the basal diet. Each 10 Gm. of ration contained approximately the amount in the daily supplement fed. No important differences in the results of the two methods of supplementation were observed.

A week or two later there was a slight loss of hair in the circumocular regions (fig. 2). In some instances it was accompanied or preceded by a slight swelling and scaling of the lids, but in other cases it appeared without apparent accompanying inflammation. The circular rim of alopecia involving and surrounding the eyelids has been referred to as "spectacle alopecia."[4] Areas of diffuse alopecia also occurred in the preauricular regions and on the sides of the snout.

After the fourth week the growth was diminished and the average gain in weight was approximately 3 to 4 Gm. per week. Symmetric patterns of grayness were observed in the fur of the circumocular regions or on the sides of the nose and the shoulders in 50 per cent of the group (fig. 3*a*). The patterns extended peripherally and sometimes involved the entire hood (fig. 3*b*). A diamond-shaped patch of fur on the vertex was usually the last to turn gray. Gradually the fur lost its luster and became coarse. Concomitantly there was a plateau or a slight decline in weight. Mild, generalized, scaly, erythematous and sometimes eczematous dermatitis was followed by diffuse loss of hair, which was most extensive on the

Fig. 2.—Circumocular alopecia.

abdomen (fig. 4*a*) and in the areas of depigmentation, particularly on the sides of the nose and in the preauricular and circumocular regions (fig. 4*b*). Scaling was especially extensive on the outer aspects of the thighs and on the back (fig. 4*c*). The sides of the snout were edematous, and there were fissures of the labial commissures. On the shoulders, on the abdomen and, to a lesser extent, on the back there were occasionally small plaques of vesiculation and crusting, which sometimes persisted after all of the other cutaneous signs had been cured. In many of the animals there were ridging and scaling of the tip of the tail with curling and contraction (fig. 5*a*). This was often so extensive that it was not possible forcibly to straighten the tail. Gangrene and amputation of the tip occurred in several animals. In the majority there was an increase in scaling of the paws and in a few, in the terminal stages, there was a slight amount of erythema of the paws. As the disease progressed the animals were weak and slightly humped. The appetite diminished. In some there was a serous discharge from the nose, and occasionally the vibrissae were stained with a sticky reddish brown material. In a few the ears were slightly erythematous and scaly just before death. Pruritus was absent or extremely mild. There were no ulcerations.

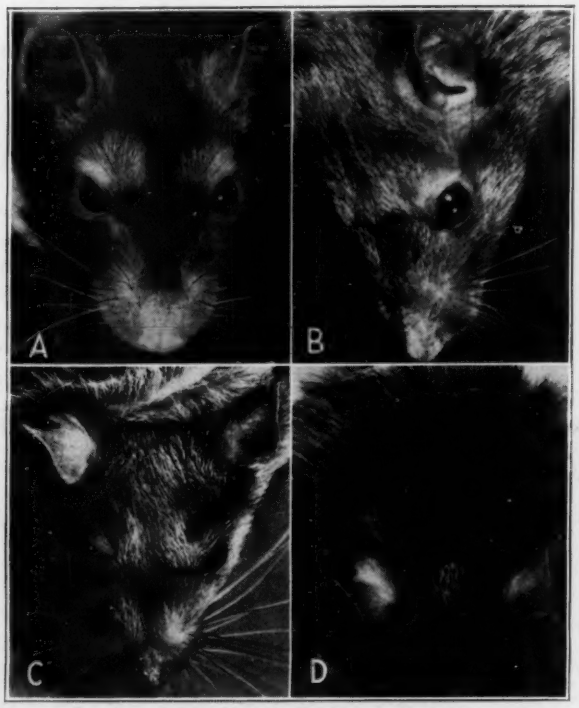

Fig. 3.—*A*, early stage of symmetric pattern grayness. *B*, advanced graying involving the entire hood. *C*, partial restoration of color after treatment. *D*, complete restoration of color except for a small area on the vertex.

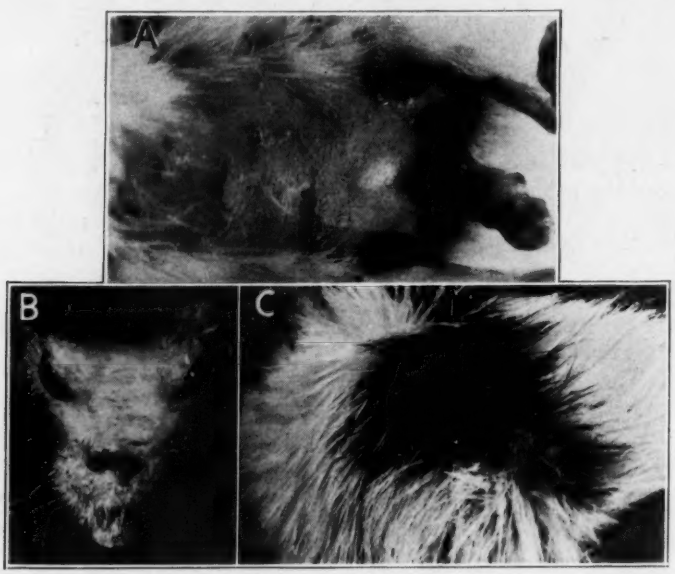

Fig. 4.—*A*, generalized alopecia and dermatitis of the abdomen. *B*, dermatitis of the region of the pattern grayness of the snout. *C*, crusting and scaling on the back.

Although a few of the rats survived for seven or eight months, the majority of them either died or were killed during the third to the fourth month. There was never a prolonged decline in the weight curve. There was no diminution in hemoglobin in the late stages of the deficiency.

Numerous sections of skin from every portion of the animals were examined. There were minor variations in the histologic alterations, and in many rats it was difficult to detect any abnormality in the early stage. The first change was slight hyperkeratosis and acanthosis. As the disease progressed there was an

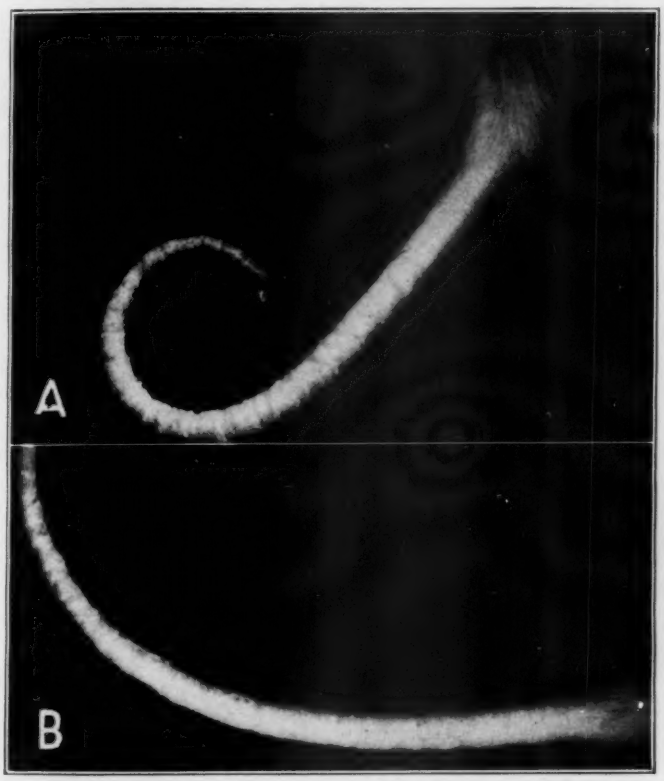

Fig. 5.—Curling, ridging, scaling and gangrene of the tail (*A*) cured by administration of crude filtrate preparation or corn oil (*B*) but unaffected by pantothenic acid.

increase in the hyperkeratosis and acanthosis, and occasionally there were parakeratosis, patchy intraepidermal vesiculation and crusting at the sites where diffuse dermatitis or small crusted eczematous plaques were observed grossly. In the late stage the epidermis was of approximately normal thickness or slightly thinner than normal. A consistent observation was a narrow, uniform follicular dilatation in which there was a widening of the follicle from the orifice to the bulb (fig. 6). There was no perifollicular cellular infiltrate. In the most advanced stages, particularly in sections from the eyelids and sides of the snout, there were slight

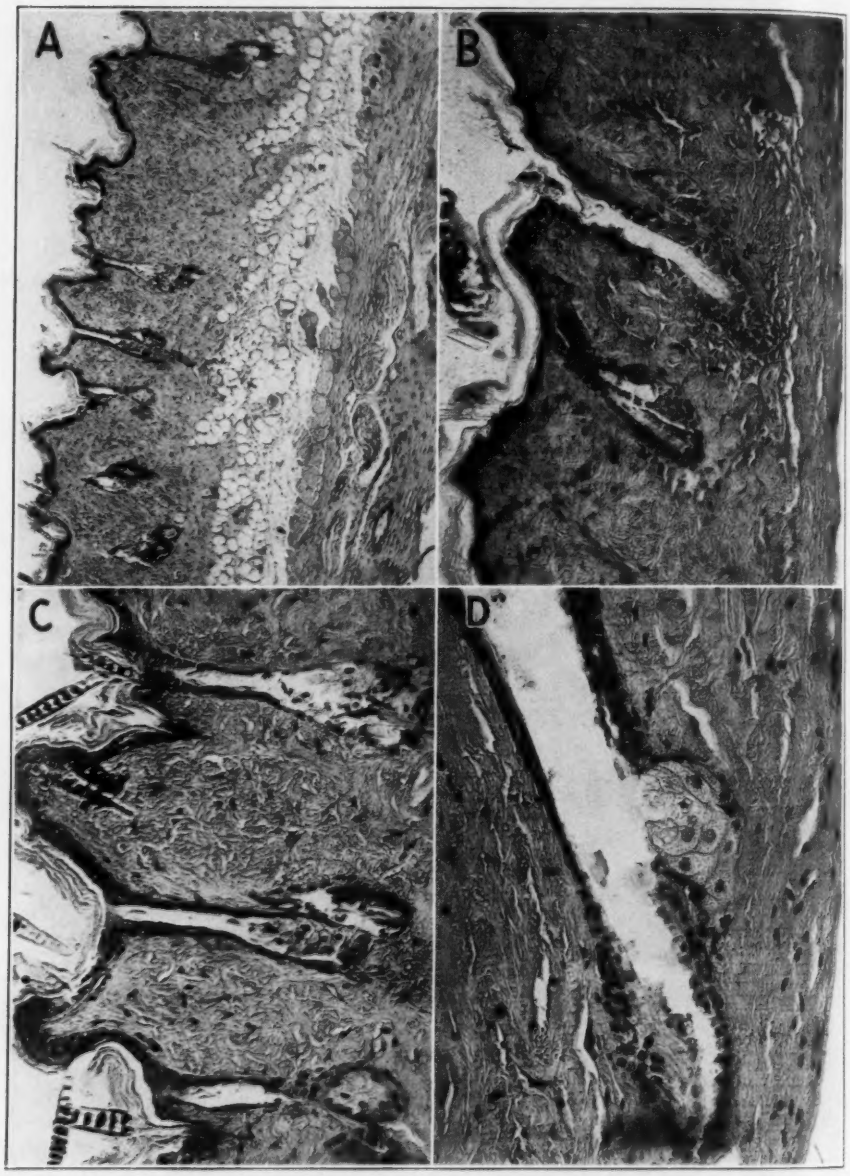

Fig. 6. — Photomicrographs showing characteristic follicular dilatation and absence of inflammation or infiltrate in the cutis. Note the approximately normal thickness of the skin and the moderate amount of subcutaneous fat in contrast to the severe atrophy which occurs in riboflavin deficiency. *A* indicates tissue from gray hood (× 27); *B*, from snout (× 155); *C*, from gray hood (× 155); *D*, from back (× 225).

diffuse mononuclear cellular infiltrate in the cutis and slight edema accompanied by dissociation of the connective tissue in the upper part of the cutis. Hyperemia was rare. The sebaceous glands remained intact until the late stages. There was no metaplasia. The cutis was of approximately normal thickness, and there was a moderate amount of subcutaneous fat. There was a loss of many hairs from the dilated follicles, and some of the sebaceous glands were shrunken and disintegrated in the late stage. There were no abscesses or areas of dense cellular infiltration. These observations contrast impressively with the microscopic appearance in riboflavin deficiency, in which there is an atrophy of the epidermis, sebaceous glands, hair follicles and cutis, with loss of subcutaneous fat. There is also a striking contrast with pyridoxine deficiency, which is characterized by acanthosis and an increase in cells of the basal layer type, intraepidermal vesiculation, edema of the cutis, diffuse cellular infiltration, some hyperemia and in the late stages polymorphonuclear cellular infiltration into the cutis and ultimately abscess formation. There was little variation in the observations of the skin in different areas of the body. Sections from the dorsa of the paws and the plantae were compared with sections from the paws of pyridoxine-deficient animals. The hyperkeratosis and mild acanthosis observed in this experiment resembled slightly the changes observed in the early stages of pyridoxine deficiency before the process had advanced to acanthosis, intradermal vesiculation and edema of the cutis.

Experiment 2.—When 100 micrograms of calcium pantothenate was fed daily to rats with the early signs described in experiment 1, the graying was cured (fig. 3*c* and *d*), growth was accelerated and the general condition improved. When it was administered to rats with fully developed generalized dermatitis, there was a dramatic involution of the dermatitis and microscopic examination showed approximately normal skin and appendages. However, the scaliness of the paws and the scaling, ridging and curling of the tail were unaffected or were accentuated and secondary graying of the fur of the head resulted.

When a daily supplement of 50 micrograms of calcium pantothenate was added to the diet and fed to a similar group of 10 young rats from the beginning of the experiment, there was a gain of at least 10 Gm. per week for four months. For the females this approximated the normal growth attained on stock rations; however, for the males the curves represented retarded growth. Mild, fine, dry scales appeared on the paws and ankles, and the distal portion of the tail was ridged, scaly and curled. The fur was normal in texture. There were no signs of alopecia, dermatitis or graying in rats observed for seven months. Sections from the trunk and head showed little if any alteration. There was no evidence of dermatitis. Even in the late stages of the experiment the epidermis, sebaceous glands and hair follicles were approximately normal and there was abundant subcutaneous fat. Sections from the paws showed mild hyperkeratosis and acanthosis. It was apparent that pantothenic acid had no effect on scaliness of the paws and scaling, ridging and curling of the tail.

Experiment 3.—In order to evaluate the effect of various supplements which have been reported to be related in one way or another to the signs described, a series of preventive and curative tests were performed. The diet described in experiment 1 was fed to a similar group of 10 young rats. From the beginning an additional supplement of impure aluminum silicate (fullers' earth) filtrate from liver was fed. It was prepared according to the method of Lepkovsky, Popper

and Evans [25] and of Jukes and Lepkovsky.[26] It was fed at a level corresponding to 1 Gm. of whole liver per rat per day.[27] The growth rate was retarded, but there was a steady gain of 5 to 10 Gm. per week for nine months. No cutaneous alterations were observed, and microscopic examination showed no important changes. Therefore, the rats that received the crude liver filtrate were protected not only against the development of dermatitis and graying but also against scaly paws and ridged, curly tails. Furthermore, when the liver filtrate was fed at a 3 Gm. level to rats described in experiment 1 after they were depleted for two months, there was a rapid gain in weight, all the cutaneous signs underwent involution and there was dramatic improvement in the general well being of the rat. No secondary or late graying was observed. Microscopically the skins were normal.

In order to demonstrate that scaliness of the paws and the described changes in the tails were not due to pyridoxine deficiency the dose of this supplement was increased to 75 micrograms per rat per day in one group of animals. This brought about no improvement. However, 0.5 cc. of corn oil per day resulted in a fairly prompt amelioration of the scaliness of the paws and curling of the tail in a similar group of animals, although it had no effect on the generalized dermatitis or graying. A somewhat slower response was obtained when the liver filtrate fraction was administered at a level of 3 Gm. of liver per rat per day, as previously described. It was evident that these signs were due to a deficiency of some additional factor present in the filtrate and in corn oil. In pyridoxine-deficient rats McElroy and Goss [28] noted the development and cure of an apparently similar lesion which they termed a "ring-tailed" condition.

There was no discernible influence on the cutaneous signs or on the growth curves and general well-being of the rats when 4 mg. of choline chloride per day was administered to rats that received the deficient diets. In a high percentage of the rats receiving no choline there was fatty infiltration of the liver.

COMMENT

It has been shown by several investigators that pantothenic acid is an important growth factor for the rat [29] and that it prevents dermatitis

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25. Lepkovsky, S.; Popper, W., and Evans, H. M.: Concentration of Vitamin G by Adsorption and Elution from Fullers' Earth, J. Biol. Chem. **108**:257 (Jan.) 1935.

26. Jukes, T. H., and Lepkovsky, S.: Distribution of the Filtrate Factor (Water Soluble Vitamin Belonging to the Vitamin B Complex and Preventing Dietary Dermatitis in Chicks) in Certain Feeding Stuffs, J. Biol. Chem. **114**: 117 (May) 1936.

27. This is equivalent to 23 micrograms of calcium pantothenate. The determination was carried out by the yeast assay method by Dr. H. J. Prebluda and Dr. H. Hodge, Research Development Laboratory, United States Industrial Chemicals, Inc.

28. McElroy, L. W., and Goss, H.: Development and Cure of "Ring-Tailed" Condition in Rats on Vitamin B_6 Deficient Diets, Proc. Soc. Exper. Biol. & Med. **45**:717 (Nov.) 1940.

29. Oleson, J. J.; Woolley, D. W., and Elvehjem, C. A.: Is Pantothenic Acid Essential for the Growth of Rats? Proc. Soc. Exper. Biol. & Med. **42**:151 (Oct.) 1939.

in the chick.[2] Hogan and Richardson,[30] Edgar and Macrae,[31] Halliday and Evans [32] and others presented evidence that rats required a growth factor in addition to thiamine, riboflavin and pyridoxine. Lepkovsky, Jukes and Krause [33] reported cutaneous changes and poor growth in rats receiving a purified diet supplemented with a vitamin B_1 concentrate, crystalline riboflavin and a rice bran eluate (pyridoxine). The eyelids of the animals were swollen and stuck together, the eyes watery and the noses inflamed. They cured the signs with the filtrate obtained after treatment of an aqueous extract of liver with impure aluminum silicate and they suggested that the rat growth factor might be identical with the "filtrate factor" which cured chick dermatitis.

György and Eckardt [34] described three types of cutaneous lesions in rats fed thiamine and riboflavin after crystalline pyridoxine was administered to cure the specific peripheral dermatitis. Some or all of the signs of the three types corresponded to various stages described in experiment 1. György, Poling and Subbarow [35] reported the cure of the three types of cutaneous lesions with a purified but still crude salt of pantothenic acid. Richardson and Hogan [36] demonstrated the effectiveness of pantothenic acid in the treatment of dermatitis of the rat. Morgan and Simms [37] described a variety of cutaneous signs, including large ulcers at the base of the tails, in groups of rats suffering from prolonged deficiency. The ulcers were cured by administration of liver, yeast or rice bran filtrate preparations. Although some of our rats survived for nine months, ulcers were never observed. Unna [38] reported scant, coarse fur showing rusty spots,

30. Hogan, A. G., and Richardson, L. R.: Skin Lesions of the Rat Associated with the Vitamin B Complex, Bulletin 241, Missouri Agricultural College, 1936.

31. Edgar, C. E., and Macrae, T. F.: The Water Soluble B Vitamins: IX. Properties of the Dietary Factor Contained in Fullers' Earth Filtrate from Autoclaved Yeast Extract, Biochem. J. **31**:893, 1937.

32. Halliday, N., and Evans, H. M.: On the Fractionation of the Vitamin B_2 Complex from Various Source Materials, J. Biol. Chem. **118**:255 (March) 1937.

33. Lepkovsky, S.; Jukes, T. H., and Krause, M. E.: The Multiple Nature of the Third Factor in the Vitamin B Complex, J. Biol. Chem. **115**:557 (Sept.) 1936.

34. György, P., and Eckardt, R. E.: Vitamin B_6 and Skin Lesions in Rats, Nature, London **144**:512 (Sept. 16) 1939.

35. György, P.; Poling, C. E., and Subbarow, Y.: Experiments on the Antidermatitis Component of the Filtrate Factor in Rats, Proc. Soc. Exper. Biol. & Med. **42**:738 (Dec.) 1939.

36. Richardson, L. R., and Hogan, A.: Relation of Pantothenic Acid to Dermatitis of the Rat, Proc. Soc. Exper. Biol. & Med. **44**:583 (June) 1940.

37. Morgan, A. F., and Simms, H. D.: Greying of the Fur and Other Disturbances in Several Species Due to a Vitamin Deficiency, J. Nutrition **19**:233 (March) 1940.

38. Unna, K.: Pantothenic Acid Requirement of the Rat, J. Nutrition **20**:565 (Dec.) 1940.

inflammation of the nose, blood-coated whiskers and hemorrhages under the skin in rats maintained on a diet devoid of pantothenic acid.

The role of pantothenic acid in the cure and prevention of nutritional achromotrichia is well known.[39] Morgan, Cooke and Davison[40] recognized that the filtrate fraction of the vitamin B complex contained a factor which prevented and cured the graying of the fur of rats. Previously Hartwell[41] had observed that the brown-black fur of pied rats turned to gray when they were fed a diet of bread and milk. The addition of casein or of casein and marmite brought about restitution of the original color. She concluded that the graying was due to deficiency of tyrosine and tryptophane. In reviewing her experiments in the light of later knowledge, we believe it is possible that the graying was due to deficiency of either anti-gray-hair vitamins or copper. In the course of assaying a wheat germ product of supposed high vitamin B concentration, Bakke, Achehoug and Zbinden[42] discovered that when the product was fed in conjunction with a basal diet to black or black and white rats, the hair turned silver gray. There was no diminution in hemoglobin. Although they postulated the presence of a toxic factor in the wheat germ, their results suggest that they were dealing with a deficiency of the anti-gray-hair factors. Gorter[43] fed a ration high in carbohydrate but low in the vitamin B complex to black and hooded rats. It was supplemented with an acid clay adsorbate (thiamine) and egg white or horse flesh (riboflavin). In two months the fur was depigmented. The color was restored slowly by feeding whole yeast. Although Gorter later[44] attributed the curative effect to the copper content of the yeast, it is possible that he also was dealing with deficiency of the anti-gray-hair factors in the vitamin B complex. Free[45] differentiated the achromotrichia due to deficiency of the vitamin B complex from the depigmentation due to deficiency of iron, copper and manganese. György[7]

39. (*a*) György, P., and Poling, D. C.: Pantothenic Acid and Nutritional Achromotrichia in Rats, Science **92**:202 (Aug. 30) 1940. (*b*) Unna, K., and Sampson, W. L.: Effect of Pantothenic Acid on the Nutritional Achromotrichia, Proc. Soc. Exper. Biol. & Med. **45**:309 (Oct.) 1940.

40. Morgan, A. F.; Cooke, B. B., and Davison, H. G.: Vitamin B_2 Deficiencies as Affected by Dietary Carbohydrate, J. Nutrition **15**:27 (Jan.) 1938.

41. Hartwell, A. C.: Notes on Colour Changes in Rats' Fur Produced by Alterations in the Diet, Biochem. J. **17**:547, 1923.

42. Bakke, A.; Achehoug, V., and Zbinden, C.: Un nouveau facteur de la nutrition, Compt. rend. Acad. d. sc. **191**:1157 (Dec. 8) 1930.

43. Gorter, F. J.: Dietary Depigmentation of Young Rats, Nature, London **134**:382 (Sept. 8) 1934.

44. Gorter, F. J.: Dietary Depigmentation of Young Black and Pied Rats Promoted by Rapid Growth, Prevented and Cured by Ingestion of Copper, Ztschr. f. Vitaminforsch. **4**:277, 1935.

45. Free, A. H.: Nonidentity of Grey Hair Produced by Mineral Deficiency and Vitamin Deficiency, Proc. Soc. Exper. Biol. & Med. **44**:371 (June) 1940.

observed bleaching in a few rats to which thiamine and lactoflavin were fed in order to produce the specific dermatitis of pyridoxine deficiency. When Lunde and Kringstad [46] fed purified diets deficient in certain members of the vitamin B complex, they observed that black hair turned gray. When diets rich in pyridoxine and low in the "filtrate factor" were fed, a symmetric graying of the fur was observed in piebald rats. Later they presented evidence which showed that the anti-gray-hair factor was present in filtrates prepared from yeast or liver.[47] When Morgan and Simms [37] fed a diet supplemented with wheat germ eluate, riboflavin and thiamine, half of the rats showed symmetric pattern graying in addition to dermatitis. Administration of liver, yeast, yeast filtrate, concentrated acid yeast eluate, liver meal, liver paste, liver filtrate, rice bran filtrate, cane molasses or alfalfa extract cured the grayness at varying rates of speed. György, Poling and Subbarow [35] showed that purified but still crude concentrates of pantothenic acid contain a factor concerned in the cure of nutritional achromotrichia of rats. Proof that pantothenic acid was an important achromotrichia factor for rats was furnished independently by György and Poling [39a] and by Unna and Sampson [39b] soon after sufficient amounts of the pure substance became available for study of its biologic activity.

Morgan and Simms [37] made histologic studies of the thyroid, adrenals, gonads and skin of filtrate-deficient rats. In animals which had grayed, the zona reticularis of the adrenals was degenerated with heavy deposits of yellow pigment and an excess of vascularity. These conditions were not pronounced in deficient animals which had not grayed and were largely remedied in those which had been cured by crude anti-gray-hair preparations. The thyroids of the grayed animals were damaged with no serration of colloid. Some acini were totally filled with epithelial cells, which indicated relative inactivity of the gland. The more advanced the graying of the hair, the more advanced was the abnormality of the thyroid. Loss of the elastic layer of the skin and failure of spermatogenesis were also noted.

Daft, Sebrell, Babcock and Jukes [48] demonstrated that repair or prevention of adrenal necrosis in rats could be achieved by a daily dose of 100 micrograms of synthetic pantothenic acid for six to fourteen days. They concluded that this was presumptive evidence that a deficiency of

46. Lunde, G., and Kringstad, H.: Ueber Veränderungen des Pelzs von Ratten durch Mangel an gewissen Factoren des Vitamin B-Komplexes: II, Ztschr. f. physiol. Chem. **257**:201, 1939.

47. Lunde, G., and Kringstad, H.: The Anti-Grey Hair Vitamin: A New Factor in the B Complex, J. Nutrition **19**:321 (April) 1940.

48. Daft, F. S.; Sebrell, W. H.; Babcock, S. H., Jr., and Jukes, T. H.: Effect of Synthetic Pantothenic Acid on Adrenal Hemorrhage, Atrophy and Necrosis in Rats, Pub. Health Rep. **55**:1333 (July 26) 1940.

pantothenic acid was at least one of the causes of adrenal lesions of rats on deficient diets. Ashburn [49] demonstrated a partial or complete adrenal cortical insufficiency, abnormal testicular function and cartilage hypoplasia in the rats of Daft, Sebrell, Babcock and Jukes. There were striking differences in the fat content, particularly in the fascicular zone of the adrenals of the deficient group and the group given a supplement of pantothenic acid. The untreated group showed depletion of fat in this layer. Mills, Shaw, Elvehjem and Phillips [50] and Salmon and Engel [51] made similar observations. We noted a high incidence of adrenal cortical necrosis in this experiment but were unable to correlate it with graying or with the severity of dermatitis.

It is evident that there is more than one factor in the vitamin B complex concerned with the prevention of graying of the hair in rats. Oleson, Elvehjem and Hart [52] observed that pantothenic acid preparations delayed the appearance of achromotrichia but failed to prevent it. Dimmick and Lepp [53] found that pantothenic acid incompletely prevented graying. Williams [54] was unable, with pantothenic acid, to cure grayness in deficient rats. Neilson, Oleson and Elvehjem [6] obtained a crystalline material from liver which prevented achromotrichia when it was fed at a level of 15 micrograms per day. It was apparently distinct from other members of the vitamin B complex. Ansbacher [18] reported that para-aminobenzoic acid cured graying observed in rats receiving adequate pantothenic acid. György and Poling [16] suggested that biotin was an additional factor associated with normal pigment metabolism under special dietary conditions.

Pattern grayness was originally observed in curative experiments of pyridoxine deficiency during the period of rapid growth which immediately followed administration of the vitamin.[46] We have observed this phenomenon of graying in curative experiments of riboflavin deficiency.[20] Graying under such circumstances proceeds more rapidly and is more uniformly obtained than under the rigid circumstances of the present

49. Ashburn, L. L.: The Effect of Administration of Pantothenic Acid on the Histopathology of the Filtrate Factor Deficiency State in Rats, Pub. Health Rep. **55**:1337 (July 26) 1940.

50. Mills, R. C.; Shaw, J. H.; Elvehjem, C. A., and Phillips, P. H.: Curative Effect of Pantothenic Acid on Adrenal Necrosis, Proc. Soc. Exper. Biol. & Med. **45**:482 (Oct.) 1940.

51. Salmon, W. D., and Engel, R. W.: Pantothenic Acid and Hemorrhagic Adrenal Necrosis in Rats, Proc. Soc. Exper. Biol. & Med. **45**:621 (Nov.) 1940.

52. Oleson, J. J.; Elvehjem, C. A., and Hart, E. B.: Nutritional Achromotrichia, Proc. Soc. Exper. Biol. & Med. **42**:283 (Oct.) 1939.

53. Dimmick, M. K., and Lepp, A.: Relation of Pantothenic Acid to the Filtrate Fraction of the Vitamin B Complex, J. Nutrition **20**: 413 (Nov.) 1940.

54. Williams, R. R.: Inefficiency of Pantothenic Acid Against Greying of the Fur, Science **92**:561 (Dec. 13) 1940.

type of experiment, wherein there is never a period of great and sudden increase in weight. Transient grayness also was observed on one occasion in this experiment during a period of rapid growth which followed the administration of pantothenic acid. The achromotrichia was of a different distribution than that observed in the other rats. It is possible that it was due to a temporary relative deficiency of additional achromotrichia factors which were present in the diet in minimal amounts.

Oleson, Bird, Elvehjem and Hart [8] showed that "spectacle eye condition" in rats could be prevented by administering corn oil. Oleson, Elvehjem and Hart [4] obtained cures by feeding a liver filtrate preparation or an inactivated pantothenic acid concentrate. Pavcek and Baum [17] cured the "spectacle eye condition" in rats by feeding them inositol. It is our opinion that circumocular alopecia with or without accompanying or preceding inflammation, or the "spectacle eye condition," is not a single specific sign of deficiency. It is often associated with dermatitis elsewhere and is not necessarily found only in vitamin B complex deficiencies. There is an objection therefore to designating any material or fraction as the "spectacle eye" factor.

There is evidence that an important relation exists between the essential fatty acids and pyridoxine. The sparing action of fats and the unsaturated fatty acids in pyridoxine deficiency has been demonstrated by several investigators.[55] Schneider, Steenbock and Platz [3a] and Supplee, Bender and Kahlenberg [3b] independently observed that in filtrate preparations there was a component distinct from pantothenic acid which acted in complementary fashion with pyridoxine to cure the scaly dermatitis of the paws which persisted in spite of pyridoxine therapy. The findings in experiment 3 clearly confirm the complex relation of unsaturated fatty acids, pyridoxine and a filtrate component. Furthermore, we have shown [22] that deficiency of these complementary vitamins, namely, pyridoxine and a factor in the filtrate, resulted in a high incidence of gangrene and amputation of the digits of rats.

Griffith and Wade [56] reported hemorrhagic degeneration of the kidneys in young rats receiving low choline diets. The lesion was

55. (*a*) Birch, T. W., and György, P.: A Study of the Chemical Nature of Vitamin B_6 and Methods for Its Preparation in a Concentrated State, Biochem. J. **30**:304, 1936. (*b*) Birch, T. W.: The Relation Between Vitamin B_6 and the Unsaturated Fatty Acid Factor, J. Biol. Chem. **124**:775 (Aug.) 1938. (*c*) Quackenbush, F. W., and Steenbock, H.: Acrodynia and the Essential Fatty Acids, ibid. **123**:xcvii (May) 1938. (*d*) Salmon, W. D.: The Effect of Certain Oils in Alleviating Localized, Erythematous Dermatitis (Acrodynia or Vitamin B_6 Deficiency) in Rats, ibid. **123**:civ (May) 1938.

56. Griffith, W. H., and Wade, N. J.: Choline Metabolism: I. The Occurrence and Prevention of Hemorrhagic Degeneration in Young Rats on a Low Choline Diet, J. Biol. Chem. **131**:567 (Dec.) 1939.

apparently similar to that described in 1929 by Cox, Smythe and Fishback,[57] who fed purified rations to which cystine had been added. György and Goldblatt[16] called attention to the role of choline as a potential member of the vitamin B complex. They observed that experimental rations commonly used in studies on the vitamin B complex were low in choline and that the addition of pyridoxine had an aggravating influence on the specific effect of choline deficiency, especially with regard to the development of cortical necrosis of the kidneys. None of our rats died from choline deficiency during the first weeks of the present experiment. Later supplementation with choline chloride reduced the incidence of fatty livers in the group receiving it. There was no discernible effect on the incidence of graying or dermatitis.

SUMMARY AND CONCLUSIONS

1. When young piebald rats were fed a purified diet low in the vitamin B complex and supplemented with synthetic forms of thiamine, riboflavin, pyridoxine and nicotinic acid, growth was retarded and the following cutaneous alterations were observed: changes in the luster and texture of the fur, mild generalized scaling, small eczematous crusted plaques, diffuse alopecia of the venter and the preauricular regions, alopecia with or without inflammation in the circumocular regions, mild diffuse scaling of the paws, scaling, ridging and curling of the tails and symmetric pattern graying of the fur of the hood. Histologically there were mild hyperkeratosis, acanthosis, occasionally parakeratosis and a slight amount of edema and vesiculation. There was a characteristic dilatation of the hair follicles. In the late stage the epidermis and the cutis were of approximately normal thickness, and there was a moderate amount of subcutaneous fat. Disintegration of the sebaceous glands occurred in the late stages in the areas of alopecia.

2. Supplementation with pantothenic acid promoted growth and prevented and cured the generalized dermatitis and the symmetric pattern grayness. It had no effect on the scaling of the paws and the ridging, curling and scaling of the tails.

3. Liver filtrate preparations prevented or cured all the cutaneous signs observed. Corn oil prevented or cured scaly paws and the scaly, ridged, curled tails but had no effect on the generalized dermatitis.

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57. Cox, G. J.; Smythe, C. V., and Fishback, C. F.: Nephropathic Action of Cystine, J. Biol. Chem. **82**:95 (April) 1929.

HISTOLOGIC EVALUATION OF THE EFFECTS OF ICHTHAMMOL

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Ichthammol is a sulfonated bitumen of complex structure. As early as 1883 Baumann and Schotten,[1] after purely chemical research, drew up an empiric formula for a sulfone compound, ammonium ichthosulfonate, which they called ichthyol (sulfonated bitumen N. F. V; ichthammol N. F. VI). Three years later Unna [2] published the first comprehensive study on its clinical application. He recommended the compound primarily for the therapy of dermatoses, but he also mentioned that it was useful when administered internally for treating gout and rheumatic conditions. It was first used in gynecologic practice by Freund [3] in 1890. Shortly thereafter Neisser [4] and Jadassohn [5] recommended it for the treatment of gonorrhea. More recently Scheibler [6] and Scheibler and

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1. Baumann, E., and Schotten, C.: Ueber das Ichthyol, Monatsh. f. prakt. Dermat. **2**:257-262, 1883.

2. Unna, P. G.: Ichthyol und Resorcin als Repräsentanten der Gruppe reizender Heilmittel, in Unna, P. G.: Dermatologische Studien, Leipzig, L. Voss, 1886, no. 2.

3. Freund, H. W.: Ueber die Anwendung des Ichthyols bei Frauenkrankheiten, Berl. klin. Wchnschr. **27**:249, 1890.

4. Neisser, A.: Ueber die Behandlung der Gonorrhoe mit Ichthyol, Internat. Dermat. Cong. (1892), Vienna, 1893, p. 303.

5. Jadassohn, J.: Ueber Behandlung der Gonorrhoe mit Ichthyol, Deutsche med. Wchnschr. **18**:850 and 871, 1892.

6. Scheibler, H.: Ueber die chemischen Bestandteile der schwefelreichen, bituminösen Teeröle (Ichthyolöle): I., Ber. d. deutsch. chem. Gesellsch. **48**:1815-1826, 1915; Ueber die chemischen Bestandteile der schwefelreichen, bituminösen Teeröle (Ichthyolöle): II., ibid. **49**:2595-2600, 1916; Ueber die Isolierung der wirksamen Schwefelkörper des Ichthyol-Rohöls und der verwandten bituminösen Teeröle, Arch. d. Pharm. **258**:70-84, 1920.

Rettig [7] showed that its therapeutic effect is due to its sulfur-containing compounds, principally thiophene homologues. In 1931 Pincussen [8] stated that one action of the substance is to effect a change in the potassium-calcium equilibrium and another is to stimulate phagocytosis.

Ichthammol is produced by the action of sulfuric acid on the sulfidic crude oil obtained by the dry distillation of a peculiar shale (*Dirschenit*) found at Seefeld, in Tirol, Austria. Sulfonation, the first step, transforms a large portion of the oil, which was originally insoluble in water, into water-soluble sulfo acids, which are characterized by the presence of the sulfonic group (SO_3H). Neutralization is then carried out with ammonia. To the sulfonated portion of the oil Unna [2] gave the name ichthyol sulfone. It has been claimed that some of the oil is present in sulfonated form in the finished product, which, however, is nevertheless clearly miscible with water. This faculty is attributed to the emulsifying action of the sulfonated portion of the oil. The ichthammol of commerce contains about 40 per cent water and some ammonium sulfate.

Analysis shows that sulfur is present in ichthammol in several forms: as ammonium sulfate, in which the sulfur is inorganically combined and has no therapeutic value; as sulfo acids, in which the sulfur in spite of its inorganic origin is organically combined and has therapeutic importance, and as thiophene homologues, in which the sulfur is of purely organic origin. The sulfur in the thiophene homologues, which originates from the bitumen of the oil shale and is present in the sulfonated as well as in the nonsulfonated portion of the preparation, is called sulfidic sulfur; and it has been stated that it is this sulfur which plays the leading role in the therapeutic action of ichthammol.

In 1933 Wernicke,[9] by a special process, produced an ichthammol preparation which was light colored and transparent. Chemical analysis showed that the composition of this compound, which he designated neoichthyol (it was also referred to as leukichthyol), was practically identical with that of the dark-colored ichthammol except for its higher content of sulfur, particularly sulfidic sulfur. In table 1 the proportions of the several forms of sulfur in the two compounds are indicated.

The present study was undertaken in an attempt to evaluate histologically the effects of these two ichthammol preparations on the skin. Extensive clinical use had given us a favorable impression of their effectiveness, but any one who has had wide experience in treating dermatoses will readily concede that it is almost impossible to evaluate

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7. Scheibler, H., and Rettig, F.: Ueber die chemischen Bestandteile der schwefelreichen, bituminösen Teeröle (Ichthyolöle): IV. Mitteilung. Ber. d. deutsch. chem. Gesellsch. **59**:1198-1202, 1926.

8. Pincussen, L.: Untersuchungen zum Mechanismus der Ichthyolwirkung, Dermat. Ztschr. **62**:258-268, 1931.

9. Wernicke, E. A.: Oelschiefer in der Medizin, Chem. Ztg. **60**:85-87, 1936.

a topical remedy by clinical applications alone. Many factors interfere with objective clinical evaluation. For example, the apparent effect of a topical application on outpatients cannot be accepted at face value because of the impossibility of supervising such patients completely. Moreover, the apparent effects on many hospitalized patients, especially those with functional and allergic dermatoses, must be accepted with reservations; such patients tend to show improvement after entering the hospital merely because they have been removed from injurious environmental influences and have benefited psychologically from turning over the responsibility of their care to the hospital staff. Consequently, the only patients suitable for study are those who are hospitalized and who have fairly generalized, symmetrically distributed dermatoses, so that when the body surface is divided longitudinally into two more or less equally involved areas for treatment the effects of two topical applications can be

TABLE 1.—*Percentage of Distribution of Three Forms of Sulfur in Ichthammol 1 and Ichthammol 2* *

	Ichthammol 1	Ichthammol 2
Dry residue, per cent	53.0	53.0
Total sulfur content, per cent	19.0	22.0
Sulfo acid sulfur, per cent	6.0	7.0
Sulfidic sulfur, per cent	10.0	12.0
Inorganic sulfur, per cent	1.5	1.5

* Since the two ichthammol preparations do not have fixed formulas, the proportions given represent the average results of analyses of a number of samples. The percentage distribution of the various forms of sulfur was determined on dried samples.

compared. Even then the evaluation of the remedy will remain subjective to a certain extent. It was such difficulties as these which made us decide to determine histologically whether cutaneous changes are produced by the application of ichthammol.

The original dark-colored ichthammol and Wernicke's light-colored compound were the preparations used.[10] Throughout this paper they are referred to as ichthammol 1 and ichthammol 2 respectively. The effects of the two ichthammol preparations were compared with those of their respective sulfones, of sulfur and of a relatively bland ointment base, an oxycholesterol-petrolatum product.[11]

EXPERIMENTAL OBSERVATIONS

The study consists of two parts; the first was carried out on animals and the second on a group of hospitalized patients.

10. The ichthammol preparations used were ichthyol and neo-ichthyol (Merck & Co., Inc.). In both the tables and the text ichthyol is designated as ichthammol 1 and neo-ichthyol as ichthammol 2.

11. Aquaphor (Duke Laboratories) was the product used.

Observations on Animals.—Material: The 8 rabbits used were divided into three groups; 4 were included in group 1, and 2 each in groups 2 and 3. The hair was clipped from several areas on each animal, and the test substances were applied daily for three weeks.

Methods: The animals in group 1 were tested with the following substances: ichthammol 1 (50 per cent in cholesterolized petrolatum), ichthammol 2 (50 per cent in cholesterolized petrolatum), precipitated sulfur (50 per cent in cholesterolized petrolatum) and cholesterolized petrolatum. The rabbits in group 2 were tested with ichthammol 1 (50 per cent in cholesterolized petrolatum), sulfone of ichthammol 1 (50 per cent in cholesterolized petrolatum) and cholesterolized petrolatum. The animals in group 3 were tested with ichthammol 2 (50 per cent in cholesterolized petrolatum), the sulfone of ichthammol 2 (50 per cent in cholesterolized petrolatum) and cholesterolized petrolatum.

At the end of the three week experimental period a specimen for biopsy was taken from each area tested. Each section was graded with regard to the presence and the degree of seven histologic features, namely, crusting, hyperkeratosis, edema of the epidermis, acanthosis, edema of the cutis, cellular infiltrate and vascular dilatation. The degree of each of these features was expressed numerically, and the figures were tabulated for each section. For each animal the tabulation for the area tested with the bland ointment base was compared with the tabulations for the areas on which other substances were used. By simple subtraction of the tabulated figures the differences between the degree of each of the seven features in the sections from the areas tested with the various substances other than the ointment base and the degree of the corresponding change in the areas to which the bland base was applied were obtained. This method is illustrated in table 2. The mean of the excess of degree of change of each of the seven histologic features in the areas treated with each of the test substances was obtained for group 1 by averaging the tabulations for each of the 4 rabbits in the group. The procedure is illustrated in table 3.

Results: The results for all three groups are given in table 4. It is evident that to some extent there was a greater degree of change in the areas treated with the five test substances than in those to which the bland ointment base was applied. The difference in degree varies with the histologic feature considered, cellular infiltration being increased the least and vascular dilatation the most. If one considers all seven of the histologic features together, the sulfur-treated areas showed the lowest mean excess degree of change and those treated with the sulfone of ichthammol 1 the highest, with the areas to which ichthammol 2, ichthammol 1 and the sulfone of ichthammol 2 were applied following in that order. All the conclusions which can be drawn from this table are included in the fore-

going statement about the relative effects of the test substances, for rabbit skin is so thin and delicate that it is entirely possible that the trauma produced by clipping the hair and applying any substance, however mild, might have been reflected in the appearance to some degree of some, if not all, of the seven histologic features which we have used as criteria. Table 5 illustrates this point, for it gives the degree of change in the areas to which only the plain ointment base was applied. Con-

TABLE 2.—*Grading* * *of Seven Histologic Features in Sections from Rabbit 3, Group 1*

	Histologic Features						
	Crusting	Hyperkeratosis	Edema of the Epidermis	Acanthosis	Edema of the Cutis	Cellular Infiltration	Vascular Dilatation
Section 568 (area treated with cholesterolized petrolatum).....	—	±	++	++	++	++	++
Section 560 (sulfur-treated area)	—	±	+++	++++	+++	++	++
Excess of degree of change in sulfur-treated area.....	0	0	+1	+2	+1	0	0

* The minus sign signifies that the feature was absent and the plus and minus sign (±) that the feature was scarcely perceptible.

TABLE 3.—*Mean Excess of Degree of Histologic Change in Areas Treated with Ichthammol 2 in Animals of Group 1*

Histologic Features	Rabbit				Mean Excess of Degree of Change
	1	2	3	4	
Crusting.....	+2	0	0	0	+0.5
Hyperkeratosis.....	+1	+1	+1	0	+0.75
Edema of the epidermis.....	+3	0	+1	0	+1
Acanthosis.....	+2	0	0	0	+0.5
Edema of the cutis.....	+1	0	+1	0	+0.5
Cellular infiltration.....	+2	0	0	0	+0.5
Vascular dilatation.....	+3	—1*	+2	0	+1

* The minus sign indicates that there was more dilatation of blood vessels in the area treated with cholesterolized petrolatum than in that tested with ichthammol 2.

sequently, we do not believe that any of the test substances can be said to have a specific effect on rabbit skin.

Observations on Hospitalized Patients.—Material: In the clinical experiment 10 patients (3 men and 7 women) were used; 9 had generalized dermatitis and 1 exfoliative dermatitis of the idiopathic type. The average period in the hospital was twenty-eight and nine-tenths days, the longest stay being sixty-two and the shortest seven days.

Methods: As in the animal experiment, several test substances were used; they were applied twice daily to symmetric, predetermined areas. Cholesterolized petrolatum was applied to the left arms and ichthammol 1

(3 per cent in cholesterolized petrolatum) to the right arms of all 10 patients. Ichthammol 2 (3 per cent in cholesterolized petrolatum) was applied to the right thighs of patients 4 to 8, and cholesterolized petrolatum was applied to the left thighs of patients 4 to 6. A specimen for biopsy was obtained from each treated area of each patient before treatment was begun and after it was completed. Nine histologic criteria were graded in the comparison of the microscopic sections, namely, hyperkeratosis, parakeratosis, width of the granular layer, intercellular

TABLE 4.—*Mean Excess of Degree of Histologic Change in Areas Treated with Test Substances in Animals of Groups 1, 2 and 3*

	Group 1			Group 2		Group 3	
Test substance	Ichthammol 1	Ichthammol 2	Sulfur	Ichthammol 1	Sulfone of Ichthammol 1	Ichthammol 2	Sulfone of Ichthammol 2
Histologic features							
Crusting	0	+0.5	0	0	0	0	0
Hyperkeratosis	+1	+0.75	+0.66	0	0	0	+0.5
Edema of the epidermis	0	+1	0	−0.5	+1	0	+1
Acanthosis	−0.33	+0.5	0	−0.5	+1.5	0	+0.5
Edema of the cutis	+1	+0.5	+0.33	0	+0.5	−0.5	0
Cellular infiltration	0	+0.5	0	−0.5	0	0	0
Vascular dilatation	+1	+1	+0.66	+1	+0.5	−1	0

TABLE 5.—*Grading of Seven Histologic Features in Areas Treated with Cholesterolized Petrolatum in Eight Animals of Groups 1, 2 and 3*

	Rabbit								Mean Degree of Change
Histologic Features	1	2	3	4	5	6	7	8	
Crusting	−	+	−	−	−	−	−	−	+0.16
Hyperkeratosis	+−	+−	+	+	+−	+−	+−	+−	+0.68
Edema of the epidermis	+	++	++	+	++	++	+	+	+1.33
Acanthosis	++	++	++	+	++	++	++	++	+1.87
Edema of the cutis	+	++	+	+	++	++	+	++	+1.33
Cellular infiltration	+	++	+	+	++	++	+	++	+1.33
Vascular dilatation	+−	++	+−	+−	++	+−	+	++	+1.16

edema of the mucous layer, intracellular edema of the mucous layer, width and acanthotic features of the mucous layer, edema of the cutis, cellular infiltration and vascular dilatation of the cutis. In each section the degree of deviation from normal of each of these nine features was determined and expressed numerically. The relative change in the degree of each of the histologic features in each area after treatment was determined by subtracting the arithmetic values for the nine features in the biopsy specimen obtained after therapy from those in the specimen from the same area before treatment. The results are shown in table 6.

The mean relative change in degree of each of the nine histologic features after treatment with ichthammol 1 and with the bland ointment

base was computed for the 10 patients. The figures are given in table 7. Corresponding relative differences after treatment with ichthammol 2 for the 5 patients who were treated with that substance were determined and the means computed. These means and the mean relative differences after treatment with ichthammol 1 and with the plain base for these 5 patients are given in table 8.

Results: Since the relative changes in degree were computed arithmetically by subtracting the values for the histologic features after

TABLE 6.—*Relative Change in Degree of Nine Histologic Features in Sections from Areas of Patient 4 Treated with Ichthammol 2*

Histologic Features	Section 274 (Right Leg Before Treatment)	Section 356 (Right Leg After Treatment)	Relative Change in Degree
Hyperkeratosis	—	+2	+2
Parakeratosis	+3	—	—3
Width of granular layer	—	+2	+2
Intercellular edema	+2	+3	+1
Intracellular edema	—	+1	+1
Width of mucous layer	—	—	0
Edema of the cutis	+4	+4	0
Cellular infiltration	+3	+2	—1
Vascular dilatation	+4	+3	—1

TABLE 7.—*Mean Relative Change in Degree of Nine Histologic Features for Ten Patients After Treatment with Ichthammol 1 and with Cholesterolized Petrolatum*

Histologic Features	Ichthammol 1	Cholesterolized Petrolatum
Hyperkeratosis	+0.1	+0.3
Parakeratosis	—1.0	+0.45
Width of granular layer	+0.6	+0.2
Intercellular edema	—0.9	—0.75
Intracellular edema	—0.3	—0.05
Width of mucous layer	0	—0.2
Edema of the cutis	—0.6	—0.85
Cellular infiltration	—0.6	—0.8
Vascular dilatation	—0.1	—0.85

therapy from similar values for the same features before therapy, the larger the negative number for the mean relative change of a given feature the nearer to normal that feature is. With this fact in mind, one can evaluate the effects of the various substances to some extent by examining and comparing the figures given in tables 7 and 8. It is evident from table 7 that the effect of ichthammol 1 on the inflamed epidermis is beneficial, for hyperkeratosis, parakeratosis and intercellular and intracellular edema were all favorably influenced. The effect on intracellular edema was most pronounced, the degree of this histologic feature being six times less after application of ichthammol 1 than after application of cholesterolized petrolatum.

The beneficial effect of ichthammol 1 on the cutis is not so evident, since the three dermal histologic features showed a reversion toward normal after application of both ichthammol 1 and cholesterolized petrolatum. The differences in degree of normalcy are probably not significant except in the case of vascular dilatation, which was definitely less after application of the bland ointment base than after treatment with ichthammol 1.

The results in table 8 differ in several respects from those in table 7. Parakeratosis and intracellular edema were favorably influenced by ichthammol 1, while the other four histologic epidermal features were not. While, as opposed to the data in table 7, ichthammol 1 had no effect on vascular dilatation, the other two dermal changes, edema and cellular infiltration, were somewhat lessened after its application. Both cholesterolized petrolatum and ichthammol 2 caused a decrease in the

TABLE 8.—*Mean Relative Change in Degree of Nine Histologic Features for Five Patients After Treatment with Ichthammol 1, Ichthammol 2 and Cholesterolized Petrolatum*

Histologic Features	Ichthammol 1	Ichthammol 2	Cholesterolized Petrolatum
Hyperkeratosis	0	+0.4	+0.4
Parakeratosis	—0.6	—1.2	—0.1
Width of granular layer	+0.2	+0.4	+0.2
Intercellular edema	0	—0.8	—0.7
Intracellular edema	—0.6	0	—0.1
Width of mucous layer	0	—0.6	0
Edema of the cutis	—0.6	—0.6	—0.7
Cellular infiltration	—0.6	—0.8	—0.6
Vascular dilatation	0	—0.4	—0.7

degree of three of the epidermal and of all of the dermal features. As opposed to ichthammol 1, both of these substances caused some decrease in vascular dilatation. Ichthammol 2 had no effect on intracellular edema, and the effect of cholesterolized petrolatum was only one-sixth that of ichthammol 1.

SUMMARY

A method is described by which the effects of cutaneous applications of test substances can be determined by an arithmetic evaluation of histologic criteria. The results of applying this method to determine the effects of two ichthammol preparations in both animal and clinical observations are reported.

The only feature which seems of significance is the distinct decrease of intracellular edema as an effect of application of ichthammol 1. Otherwise the study shows no significant trends for the results of treatment with either ichthammol preparation.

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INTRAVENOUS DRIP METHOD IN INTENSIVE ARSENOTHERAPY OF SYPHILIS

WITH PARTICULAR REFERENCE TO ITS APPLICATION FOR LATENT SYPHILIS AND FOR LATE STAGES OF THE DISEASE

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After the observations of Hyman, Chargin, Rice and Leifer [1] on the massive dose chemotherapy of early syphilis by the intravenous drip method were published, a study was undertaken in Sing Sing Prison applying this procedure to the treatment of other than the early stages of the disease. With the encouragement and supervision at its inception by the Mount Sinai Hospital group, this investigation was begun in November 1939. Although the work is incomplete, a preliminary report is herein rendered to indicate the nature of my experience to date without any evaluation of the therapeutic efficacy of the procedure.

The syphilis clinic of Sing Sing Prison Hospital seemed admirably suited for such a study. About 350 men with syphilis are admitted to this clinic each year, the majority of whom remain under incarceration for a minimum of two years while many are confined for ten years or longer. This arrangement therefore would insure an adequate follow-up period of observation, during which necessary information could be obtained to evaluate properly the results of treatment, especially in patients with latent syphilis and in late stages of the disease.

METHOD

The technic was essentially similar to that described by Hyman, Chargin, Rice and Leifer.[1] Instead of preparing a fresh solution of the arsenical to be added to the open Kelly flask at hourly intervals, I employed a 2,000 cc. vacoliter [2] to which was added at the start of the infusion the entire amount of the arsenical to be administered on any one day. The infusion was regulated so as to require nine to twelve hours to be completed. Mention of this method has been made by

From the Syphilis Clinic, Sing Sing Prison Hospital, and the Department of Medicine, New York University College of Medicine.

1. Hyman, H. T.; Chargin, L.; Rice, J. L., and Leifer, W.: Massive Dose Chemotherapy of Early Syphilis by the Intravenous Drip Method, J. A. M. A. **113**:1208 (Sept. 23) 1939.

2. Supplied for this study by a grant from Baxter Laboratories, Inc.

Leifer.[3] The arsenical employed in the treatment of all the patients was mapharsen,[4] and the amount of drug added to the infusion on any one day varied from 150 to 400 mg. The vehicle was 5 per cent, 2.5 per cent or 1 per cent dextrose solution, saline solution or one-sixth molar solution of sodium lactate.

Fig. 1.—Photograph illustrating the relative comfort and freedom of a patient receiving massive dose marpharsen therapy with the use of a prepared vacoliter and with the needle inserted into a vein of the forearm.

When intensive arsenotherapy alone was employed, the mapharsen was given in five consecutive daily infusions. In addition, patients were

3. Leifer, W.: Massive Arsenotherapy in Early Syphilis by the Continuous Intravenous Drip Method: Technic, Arch. Dermat. & Syph. **42**:246 (Aug.) 1940.

4. Supplied for this study by a grant from Parke, Davis and Company.

treated with a combination of intensive arsenotherapy by the intravenous drip method together with a varying amount of fever therapy produced by the intravenous injection of typhoid vaccine [5] or malaria organisms (tertian or quartan). Graphic representation of data on a patient treated by intensive arsenotherapy alone is shown in figure 2. The number of typhoid vaccine paroxysms varied from one to eight and were always so administered that two or three days of massive dose arsenotherapy was immediately followed by fever therapy. Graphic representation of a patient treated by this method is shown in figure 3.

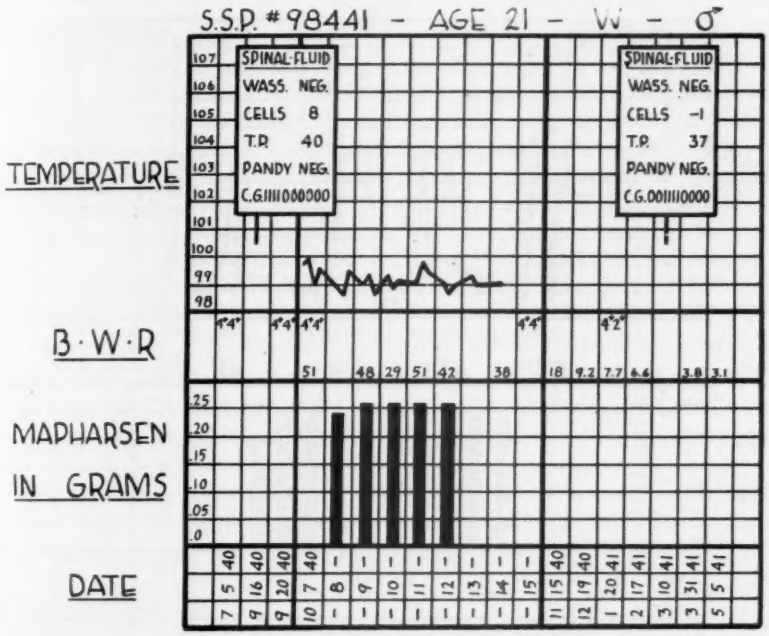

Fig. 2.—Graphic protocol of a patient who received massive dose mapharsen therapy (1,280 mg.) by the intravenous drip method. The Wassermann reaction of the blood (B. W. R.) is recorded in qualitative and quantitative titers.

Patients with syphilis who received intensive arsenotherapy did so voluntarily after they were selected to receive this treatment by the examining physician. In addition to selection on the basis of medical indications regarding the need for antisyphilitic therapy, patients were selected on the basis of the probable duration of their incarceration, administrative decisions in connection with their crimes and their psychologic suitability for prolonged investigation.

From November 1939 until July 1941 a total of 117 patients were treated by massive dose mapharsen therapy by the drip method and

5. Supplied for this study by the New York State Department of Health.

75 patients by a combination of massive dose arsenotherapy and fever therapy. All the patients were first examined in the clinic for ambulatory patients with syphilis, where a detailed history was taken and a physical examination was done. At that time data were obtained as to previous Wassermann reactions of the blood, spinal fluid analyses and treatment.

All patients were admitted to the hospital for intensive antisyphilitic therapy. A routine laboratory examination, consisting of a Wassermann test performed in our own laboratory and in the laboratories of

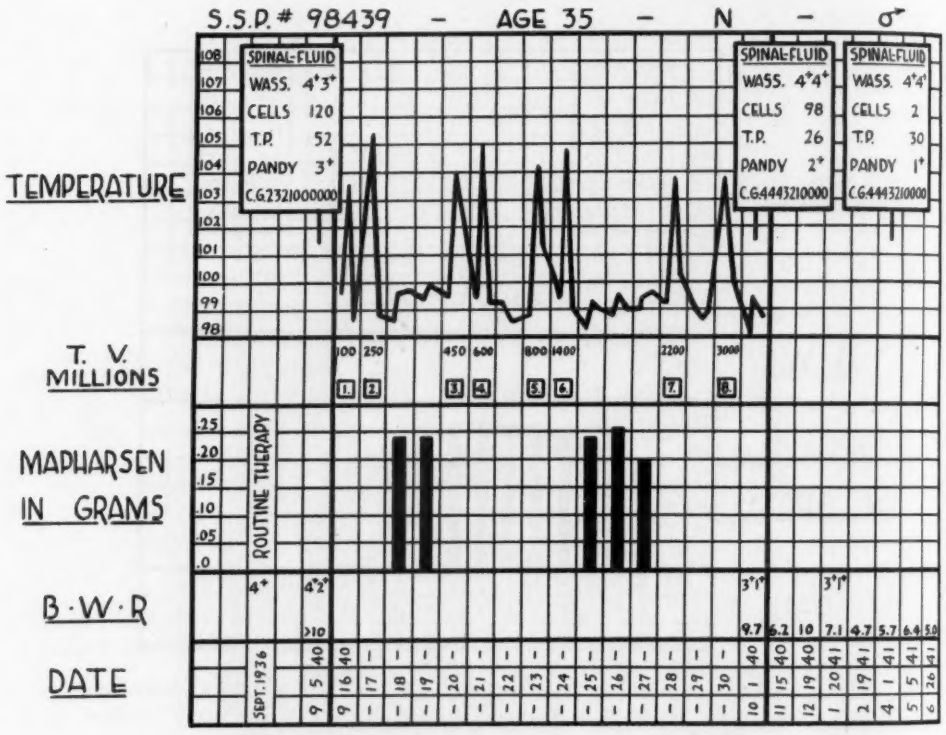

Fig. 3.—Graphic protocol of a patient who received combined massive dose mapharsen therapy (1,180 mg.) and underwent eight paroxysms of typhoid vaccine (T. V.) fever therapy. The estimated number of organisms in the typhoid vaccine injected is recorded. The Wassermann reaction of the blood (B. W. R.) is recorded in qualitative and quantitative titers.

the New York State Department of Health, where quantitative titers were determined, a complete blood count, a urinalysis, a spinal fluid analysis, a serum bilirubin determination, and taking of an electrocardiogram, a stethogram and a teleroentgenogram, was made in each case prior to administering the intensive arsenotherapy. During the course of intensive therapy, frequent urinalyses were made, and each

patient had two or more complete blood counts after treatment. Analysis of the spinal fluid was performed every six months after treatment for those patients whose pretreatment fluid was found to be abnormal. Twenty-three patients whose initial fluids were essentially normal had a repeat analysis subsequent to treatment. Frequent determinations of the Wassermann reaction of the blood were made during the course of intensive arsenotherapy, and in 101 patients this was done daily throughout the period of hospitalization. Serologic follow-up studies were made every month when possible. Reexamination of the patients who remained under incarceration in Sing Sing Prison was performed by me. Those who were transferred to other state institutions or discharged on parole since this study began were examined by other physicians. Whenever possible it was arranged to have the patient who received intensive therapy remain in Sing Sing Prison for follow-up observation during his period of incarceration. However, there were 16 patients who were transferred to other state institutions, where their subsequent examinations were performed.

In 84 persons a varying amount of bismuth, injected either as the subsalicylate in oil or as lipo-bismol,[6] was administered in weekly injections just prior to the giving of intensive arsenotherapy. Except for 9 patients who received subsequent routine antisyphilitic therapy from other physicians after leaving Sing Sing Prison and for 14 who for various reasons were retreated by intensive methods, no patient received any further antisyphilitic therapy.

RESULTS

Of the 117 patients treated by intensive massive dose mapharsen therapy alone and the 75 patients treated by a combination of intensive arsenotherapy and fever therapy, there were 14 patients who during the course of this study were retreated, making a total of 206 instances in which intensive antisyphilitic therapy was administered to 192 patients. All patients were males between the ages of 18 and 63. There were 126 Negroes, 65 white persons and 1 Chinese. To these were administered varying amounts of mapharsen; the distribution of total amounts are indicated in table 1. One patient was retreated by a combination of mapharsen and fever therapy eight months after receiving intensive massive dose arsenotherapy, and received a total of 2,680 mg. of mapharsen during these two courses. Of the 89 instances in which intensive arsenotherapy was given combined with artificial fever therapy, from five to eight paroxysms were produced in 75 while the remainder had less than this number.

A tabulation of the type of syphilitic disease exhibited by this group of patients and the method by which they were treated is seen in table 2.

6. Supplied for this study by Parke, Davis and Company.

It is conceded that in many instances inaccuracy exists in the determination of whether a patient is in the early or late stage of latent syphilis when a definite confirmed previous history is lacking. Primary syphilis is uncommon in the population considered in this study because of a considerable period of incarceration which usually precedes admission to the state prisons. There were 73 patients who had some alteration in their cerebrospinal fluid. Of these, 17 presented clinical evidence of neurosyphilis, but in table 2 the grouping of all patients

TABLE 1.—*Summary of Methods and Therapy*

Patients given massive dose mapharsen therapy by the intravenous drip method	117
Patients given combined mapharsen drip therapy and fever therapy	75
Patients retreated by combined fever therapy and mapharsen drip therapy	14
Total courses of intensive antisyphilis therapy	206
Total amount of mapharsen given during each course of therapy:	
1,000 mg. or less	15
1,001-1,200 mg.	76
1,201-1,400 mg.	61
1,401-1,600 mg.	54

TABLE 2.—*Type of Syphilis in One Hundred and Ninety-Two Patients and Method of Therapy*

Diagnosis *	Received Massive Dose Mapharsen Therapy by the Intravenous Drip Method	Received Combined Fever Therapy and Mapharsen Therapy by the Drip Method
Seropositive primary syphilis	2	0
Early latent syphilis	18	10
Late latent syphilis	62	24
Neurosyphilis †		
Group 1	2	0
Group 2	24	23
Group 3	8	16
Cardiovascular syphilis	0	3
Congenital syphilis	1	1
Syphilis with associated nonsyphilitic organic disease	16	9

* Distribution of the incidence of the various stages of syphilis in this group was governed by the selection of patients for intensive therapy and does not represent a distribution in a consecutive group of persons with syphilis.

† Grouping made according to severity of alterations in the spinal fluid.

was made in accordance with the quantitative changes in the spinal fluid similar to that employed in Moore's classification.[7] This was preferred to merely indicating whether or not the patient was asymptomatic, as such a division is entirely dependent on the diagnostic ability of the examining physician and lacks objectivity. A subsequent report is intended to cover the application of intensive methods in the treatment of this group. Twenty-five patients with various stages of syphilis associated with concomitant nonsyphilitic diseases were given intensive

7. Moore, J. E.: The Modern Treatment of Syphilis, Springfield, Ill., Charles C. Thomas, Publisher, 1933.

therapy for their syphilis. Cardiovascular syphilis was present in 3 patients, who received intensive therapy.

Table 3 summarizes the observations on the toxic manifestations following massive dose mapharsen therapy in this group of 192 men.

TABLE 3.—*Toxic Phenomena in One Hundred and Ninety-Two Patients*

Toxic Manifestations	Massive Dose Mapharsen Therapy by the Drip Method (117 Patients)		Combined Fever and Mapharsen Therapy (75 Patients)	
	Number	Per Cent	Number	Per Cent
Primary fever *	18	15.4	5	6.6
Secondary fever *	16	13.6	2	2.6
Peripheral neuritis	8	6.8	4	5.3
Toxicoderma	5	4.3	0	....
Gastrointestinal symptoms	52	44.4	37	49.3
Headache and dizziness *	44	37.6	30	40.0
Local venous reactions	94	80.3	58	77.3
Renal damage	0	....	0	....
Blood dyscrasia	0	....	0	....
Jaundice	0	....	0	....
Hemorrhagic encephalitis	0	....	0	....
Exfoliative dermatitis	0	....	0	....
Fatality	0	....	0	....

* The evaluation of these toxic manifestations in patients who received combined fever and drip therapy was difficult because of the similarity to such symptoms due to fever therapy alone. The effort was made to determine the incidence of symptoms due directly to arsenotherapy.

TABLE 4.—*Summary of Follow-Up Status*

	Patients	
	Number	Per Cent
Total number of patients	192	100.0
Total now under follow-up observation	187	97.4
Now followed in Sing Sing Prison	160	83.3
Now followed in other state institutions	16	8.3
Now followed on parole	11	5.7
Lost from follow-up observation	5	2.6

TABLE 5.—*Reason for Retreatment of Fourteen Patients* *

Failure to correct reaction of spinal fluid † by massive dose mapharsen therapy (drip method)	8
Failure to correct reaction of spinal fluid † by combined fever and mapharsen therapy	2
Attempt further to decrease the titered Wassermann reaction of the blood after the mapharsen therapy (drip method)	4

* All retreatment courses were combined fever and mapharsen therapy.
† Spinal fluid revealed evidence of active syphilis six months after treatment.

Primary fever, secondary fever, peripheral neuritis and toxicodermas were observed, but no other serious immediate or late toxic manifestations occurred. Headache, nausea and vomiting were frequent, as were local signs and symptoms of venous spasm and thrombophlebitis at the site of infusion. There was no fatality in this group. With a single exception, peripheral neuritis was observed only in patients who had

received in excess of 1,200 mg. of mapharsen, and in all but 3 instances it was of an evanescent type manifested by paresthesias and tenderness of the calf coming on two to four weeks after treatment and having a duration of one to two months. In 3 instances there has remained objective evidence of peripheral neuritis one year after intensive arsenotherapy with 1,400, 1,500 and 1,500 mg. of mapharsen, respectively.

Of the entire group of 192 patients, 187 are still under observation at the time of writing while only 5 have been lost from follow-up study (table 4). Fourteen patients were retreated by combined fever and mapharsen therapy during this investigation, and the reasons for this additional treatment are summarized in table 5.

COMMENT

Intensive methods for antisyphilitic therapy by the massive dose infusion of mapharsen with or without fever therapy seem applicable for study in the treatment of persons with latent syphilis and in the late stages of the disease. Although varying amounts of mapharsen up to 1,600 mg. have been administered in a five day period, serious toxic sequelae have not been observed. In addition, minor changes in prearranged schedules of treatment for any one patient have been made infrequently, and only twice have patients been encountered who elected to abandon this form of therapy after one or two days because they were unwilling to submit to the discomfort which they claimed to experience. It should be stated, from the standpoint of the patients, that practically all are eager to take either method of intensive therapy in preference to routine therapy. Although this ought not to be a foremost consideration, it certainly must be seriously weighed when one considers the fact that even among incarcerated persons with syphilis who take treatment for their disease on a voluntary basis, delinquency and refusal to take treatment average 30 per cent in our routine ambulatory group.

Considerably more time for follow-up observation is absolutely essential in order to evaluate the therapeutic efficacy of intensive methods in the treatment of those stages of syphilis demonstrated by the group of patients reported on in this communication. For this reason, any evaluation of results in terms of "cure" or improvement, reversal of serologic reactions or changes in the spinal fluid was not made. Our observations have, however, been encouraging enough to warrant further investigation and study of additional patients. It is anticipated at present to submit more detailed reports on the progress of this study, especially as it will apply in the future to observations on therapeutic efficacy. This preliminary report is intended to make available to others the experiences which my associates and I have encountered in the

treatment of 190 patients with other than primary syphilis and to record the fact that 192 patients have received two hundred and six courses of intensive antisyphilitic therapy with massive doses of mapharsen by the intravenous drip method without a serious toxic reaction or fatality.

SUMMARY

1. One hundred and ninety-two patients with syphilis received two hundred and six courses of intensive antisyphilis therapy. All but 2 of these patients were in the latent or late stages of the disease.

2. One hundred and seventeen patients received massive dose mapharsen treatment by the intravenous drip method, and 75 patients received massive dose mapharsen treatment by the intravenous drip method together with fever therapy produced by intravenous injection of typhoid vaccine or malaria organisms.

3. No serious toxic reaction or fatality was observed in this group, but minor toxic reactions were common.

Drs. Hyman, Chargin and Leifer rendered early assistance in this study. Drs. Evan W. Thomas and Bernhard Dattner offered helpful suggestions. William S. Taylor, R.N., supervised the nursing care. The opportunity to perform this investigation was made possible by Warden Lewis E. Lawes and Dr. Charles C. Sweet, Chief of Staff.

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TREATMENT OF SCABIES WITH ROTENONE

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There is still room for improvement in the treatment of scabies. Many of the specific remedies are too odorous or greasy for comfort; others act too slowly. Some are ineffective in combating the frequently accompanying pyoderma. Their use therefore necessitates a delay until the pyogenic complications are brought under control. One hundred per cent cures are not to be expected with any preparation. When used by susceptible patients, many lead to severe dermatitis venenata, and this may prove more resistant and troublesome than the original "itch."

For these reasons rotenone ($C_{23}H_{22}O_6$) has been investigated as a remedy for scabies. This substance is derived from derris root (Derris elliptica) or from South American cube root (Lonchocarpous nicou). It is said that the natives of the Amazon valley have employed it for many years in the treatment of all types of parasitic dermatoses.

Fifty consecutive patients with scabies were treated by the local application of 2 per cent rotenone in a mucilage of quince seed, Irish moss and chloroform.[1] Patients in whom Acari could not be demonstrated microscopically or in whom the clinical manifestations were not typical were not included. About one third of the patients were children under 10 years of age.

The patients were instructed to take a warm bath and then to apply the lotion all over the trunk and extremities. This was repeated twice a day without subsequent bathing until the completion of therapy. At first the treatment was applied on two successive days, as recommended by the manufacturer of the lotion and by Thomas and Miller.[2] However, it was soon found that the routine use on four successive days led to more satisfactory results. Boiling of the clothes and other prophylactic measures were advised.

The advantages of the rotenone lotion are as follows: It is a reasonably active agent. The application of a lotion is obviously more pleasant

1. The preparation (known as ronone lotion) was furnished by the Abbott Laboratories.

2. Thomas, C. C., and Miller, E. E.: Rotenone in the Treatment of Scabies, Am. J. M. Sc. **199**:670 (May) 1940.

than the use of an ointment. The odor is negligible, a relief to those accustomed to sulfur preparations. The remedy can be used full strength for children. It can be employed in the presence of a mild dermatitis due to sulfur or benzyl benzoate. It can also be used in the rare instances in which the eruption is resistant to other specific parasiticides.

Among the disadvantages are that most patients require four days for a cure and that the drug may lead to the development of a secondary contact dermatitis. In most instances this complication is manifested by some erythema, dryness and desquamation of a minor degree. However, in 2 cases a severe generalized patchy erythematous eruption developed with weeping of the involved areas. Severe pruritus accompanied this type of reaction.

In 1 case, in which a rather severe secondary dermatitis developed, a patch test with this lotion resulted in a 4 plus reaction. In addition, thirty-six hours after the application of the test and while the patch was still in place, a severe headache, abdominal cramps and tenderness, generalized muscular aches, nausea and vomiting and a feeling of fever developed. This attack lasted sixteen hours. The patient stated that there had been no previous similar incident. This case will be reported more fully in a future paper on untoward reactions to patch tests.

Rotenone is also used as a constituent of many flea powders and agricultural insecticides. Like pyrethrum, it is said to be capable of causing dermatitis industrialis.[3] This poison also produces toxic systemic symptoms in animals.[2] However, evidence of internal complications has not followed the local application of 10 per cent rotenone ointment in man.[2]

The eruption may fail to respond to rotenone therapy. This occurred in nearly 15 per cent of my cases, which represents too high a ratio of unsatisfactory results. On the other hand, 24 patients were treated by Thomas and Miller,[2] and there were no failures. Perhaps the difference in the two series can be credited to nursing care. Saunders,[4] employing 3 per cent derris root in water and soap chips, secured good results in 90 patients with scabies. This preparation is different from that investigated in this study and contains only 0.3 per cent rotenone.

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3. Rachouchot: Plants Containing Rotenone, Occupational Dermatitis, Arch. d. mal. profess. **2**:149 (March-April) 1939.

4. Saunders, L.: The Derris Root Treatment of Scabies, Brit. M. J. **1**:624 (April 26) 1941.

The most serious objection to the use of the 2 per cent lotion of rotenone is its ineffectiveness in combating the complicating pyoderma. Although this result is in contradistinction to that of Thomas and Miller,[2] I am unable to offer any futher explanation for this discrepancy.

SUMMARY

Fifty ambulatory patients were treated by the local application of a 2 per cent rotenone lotion with 15 per cent of failures. About one third of the patients were under 10 years of age.

The advantages and disadvantages of this type of therapy for scabies are discussed.

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CHICK EMBRYO ANTIGEN

INTRAVENOUS USE IN DIAGNOSIS OF LYMPHOGRANULOMA VENEREUM

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The intravenous injection of human Frei antigen as a diagnostic test for lymphogranuloma venereum was introduced by Hellerström in 1931.[1] Its value was confirmed by Gay Prieto and Egea Bueno[2] and by Flandin and Turiaf.[3] Ravaut, Levaditi and Maisler[4] reported similar results from the use of mouse brain antigen intravenously, and Decker, Canizares and Reider,[5] in a previous report from this clinic, stated that 0.1 cc. of mouse brain antigen injected intravenously produced a thermal response which could be used as an aid in diagnosis of this disease.

During the past eight months we have studied the thermal response in 24 cases of lymphogranuloma venereum and in 24 control cases after the intravenous injection of 0.1 cc. of chick embryo antigen. Thermometric readings were taken every two hours for forty-eight hours after the injection was given. Each patient also received 0.1 cc. of chick embryo antigen control, 0.1 cc. of mouse brain antigen and 0.1 cc. of mouse brain control intravenously. Sixteen patients received in addition 0.1 cc. of a potent human antigen. Each injection was

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Lygranum was the chick embryo antigen used in this study; it was supplied by E. R. Squibb & Sons.

1. Hellerström, J., in discussion on Fernet, P.: Le traitement radiothérapique de la lymphogranulomatose inguinale subaiguë, Bull. Soc. franç. de dermat. et syph. **38**:585-588 (April) 1931.

2. Gay Prieto, J., and Egea Bueno, L.: Nueva contribución al estudio de las hemorreacciones específicas con antígeno de Frei: Su valor terapéutico, Actas dermo-sif. **27**:3-15 (Oct.) 1934.

3. Flandin, C., and Turiaf, J.: L'hémo-réaction de Ravaut dans la maladie de Nicolas-Favre, Bull. Soc. franç. de dermat. et syph. **43**:329-333 (Feb.) 1936.

4. Ravaut, P.; Levaditi, C., and Maisler: La valeur diagnostique et thérapeutique des injections intraveineuses du virus de la maladie de Nicolas-Favre d'origine simienne, Bull. Soc. franç. de dermat. et syph. **39**:1262-1266 (July) 1932.

5. Decker, D.; Cañizares, O., and Reider, R.: Mouse Brain Antigen: Intravenous Use in Diagnosis of Lymphogranuloma Venereum, Arch. Dermat. & Syph. **40**:397-401 (Sept.) 1939.

given no sooner than forty-eight hours after the preceding one, and if a thermal response was obtained from any injection the subsequent one was not given until the temperature had returned to normal and remained at that level for forty-eight hours.

We have used the same criteria for the interpretation of the tests as were reported in the previous paper from this clinic, and a "positive reaction was considered to be one in which the temperature reached 101 F. or higher for twelve hours or more." [5]

RESULTS

Intravenous Injection of Chick Embryo Antigen.—Twenty-four patients with lymphogranuloma venereum received 0.1 cc. of chick embryo antigen intravenously. Eleven gave positive thermal reactions, and 13 failed to give any reaction.

Twenty-four control patients received 0.1 cc. of chick embryo antigen intravenously. None gave a positive response.

Intravenous Injection of Chick Embryo Antigen Control.—No positive reactions were obtained in either the 24 cases of lymphogranuloma venereum or the 24 control cases when 0.1 cc. of chick embryo antigen control was injected intravenously.

Intravenous Injection of Mouse Brain Antigen.—Twenty-three patients with lymphogranuloma venereum gave positive thermal reactions to the intravenous injection of 0.1 cc. of mouse brain antigen. Only 1 patient failed to give a positive response.

Twenty-four control patients gave no response to the intravenous injection of 0.1 cc. of mouse brain antigen.

Intravenous Injection of Normal Mouse Brain Emulsion.—Twenty of the 24 patients with lymphogranuloma venereum gave negative reactions to the intravenous injection of 0.1 cc. of normal mouse brain emulsion. The other 4 gave positive reactions.

None of the 24 control patients gave positive reactions to the intravenous injection of 0.1 cc. of mouse brain control.

Intravenous Injection of a Human Antigen.—Sixteen patients with lymphogranuloma venereum who had previously given strongly positive reactions to intradermal tests received 0.1 cc. of a human antigen intravenously. None of them showed a positive thermal response.

COMMENT

Sulkin, Fletcher, Huber and Reh [6] and Combes, Cañizares and Morris [7] showed that the cutaneous reaction obtained from the intradermal

6. Sulkin, E.; Fletcher, P.; Huber, E., and Reh, P.: The Frei Test for Lymphogranuloma Venereum: Experiences with a New Antigen (Lygranum) Prepared from Infected Yolk Sac of Developing Chick Embryo, J. A. M. A. **116**: 2663 (June 14) 1941.

7. Combes, F. C.; Cañizares, O., and Morris, G.: Chick Embryo Antigen: Intradermal Use in the Diagnosis of Lymphogranuloma Venereum, to be published.

injection of 0.1 cc. of chick embryo antigen compares favorably with that obtained when a similar amount of mouse brain antigen or human antigen is injected intradermally. We expected, therefore, that the responses to the intravenous injections of these substances might parallel each other in a similar manner. This, however, is not the case, for only 11 of 24 patients (45.8 per cent) with lymphogranuloma venereum gave positive responses to the intravenous injection of the chick embryo antigen, while 23 (95.8 per cent) gave positive responses to the intravenous injection of mouse brain antigen. Such a low incidence (45.8 per cent) of positive reactions to the intravenous injection of chick embryo antigen forces us to consider this substance unsuitable as a diagnostic measure in this regard.

It is noteworthy that this negative response to the intravenous injection of chick embryo antigen was obtained in patients who gave a positive reaction to the intradermal injection of this antigen. In a similar fashion, these patients gave positive reactions to cutaneous tests but negative reactions to intravenous tests with a human antigen. These results indicate that the mechanism involved in the production of the cutaneous reaction is independent of that involved in the production of the thermal reaction.

The high percentage of positive reactions (95.8 per cent) obtained from the intravenous injection of mouse brain antigen confirms the previous report [5] that this test can be used as a diagnostic measure in cases of suspected lymphogranuloma venereum. In all cases an injection of normal mouse brain emulsion must be given as a control, for in this series in 4 of 24 cases there also was a thermal response to the injection of the normal mouse brain emulsion.

CONCLUSIONS

1. Chick embryo antigen is not reliable as an intravenous test agent for the diagnosis of lymphogranuloma venereum.

2. Mouse brain antigen is reliable as an intravenous test agent for the diagnosis of lymphogranuloma venereum.

3. The mechanism involved in the production of the cutaneous reactions to the Frei antigens is independent of the mechanism which produces the thermal response to those antigens.

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TUBERCULIN TREATMENT OF ACNE VULGARIS IN TUBERCULOUS PATIENTS

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In caring for the cutaneous disturbances of patients in the City of Chicago Municipal Tuberculosis Sanitarium we encounter acne vulgaris far more often than any other disease of the skin. This is because the patients are selected because of their youth as the ones likely to receive the greatest benefit from care in the institution. Many of them coming for treatment state that they never had acne before or that an eruption existing before their admission to the hospital has grown much worse since they entered. This we have ascribed to the fattening diet in use.

Von Kémeri [1] in 1934, on the assumption that acne vulgaris is due to focal infection, noted that many patients were not cured by eradication of all easily reached infectious foci, such as those in the tonsils and about the teeth, looked for deeper foci and found them in the lungs as foci of tuberculosis. In 52 patients all of the type described by Hollander [2] as "thin anemic undernourished patients whose thyroid gland activity is increased in a compensatory measure to cope with the endocrine imbalance produced by the gonad activity, practically thyroid toxicosis," von Kémeri observed pulmonary shadows; 23 of them had a slight excess of temperature, and all had a positive von Pirquet reaction. Forty-three of them had had tonsillectomies, and one hundred and seventy-three teeth had been extracted. After this in 22 of them the condition cleared without further treatment. The remaining 30 were treated with tuberculin, and 27 of them were cured. Von Kémeri thought acne vulgaris was a consequence of the combined action of tuberculous and other foci, the tuberculosis furnishing the chronicity and the other infection producing the activity. The activity of pulmonary foci is shown, according to him, by the signs found on auscultation and percussion, by roentgenography and by the presence of cutaneous lesions.

1. von Kémeri, D.: Aetiologie und allgemeine Behandlung der Akne vulgaris, Dermat. Wchnschr. **98**:237 (Feb. 24) 1934.

2. Hollander, L.: The Role of the Endocrine Glands in the Etiology and Treatment of Acne, Arch. Dermat. & Syph. **3**:593 (May) 1921.

Enthusiastic over this, Van Studdiford [3] made tuberculin tests in 25 patients whose chests showed no evidence of tuberculous involvement, and after removable septic foci had been eradicated and menstrual disturbances corrected, he treated them with cautious injections of tuberculin. Their dietary restrictions as to sugar and fats were removed. Three of them had tuberculous axillary glands. From the acne lesions of 2 of them the bovine type tubercle bacilli were cultured. Some were treated for six months and then given a rest from treatment; others kept up the treatment until they were well. Counting out 2 of the 25 who had roentgen treatment with the injections of tuberculin, 8, or 35 per cent, were cured and the other 65 per cent were improved.

Dealing as we do with a group of acne patients with severe pulmonary tuberculosis, we thought to discover whether careful tuberculin treatment would benefit them. Such help we need, for restriction of diet for these patients is obviously impossible and some of them are so ill that we hesitate to ask them to expend the energy necessary to do the amount of scrubbing usually demanded of acne patients.

METHOD OF STUDY

Technic.—The patients were tested first with old tuberculin 1:100,000 intracutaneously. If the results were negative in forty-eight hours, 1:10,000 and 1:1,000 solutions were used seriatim. Treatment was given subcutaneously beginning with the weakest dilution which elicited a positive cutaneous reaction. Injections were given twice weekly, increasing the dose each time to the point of giving a small local but no focal or general reacton. When a definite lump was found at the site of injection, the same dose was repeated until it failed to react. About twenty injections were given to each patient, thus covering a period of about three months of observation.

Subjects.—All patients had active tuberculosis, the condition in most of them being classified as "far advanced" (National Tuberculosis Association). All were ambulatory and afebrile as a rule. The number treated was 11. The highest dose given was 0.3 cc. of 1:1,000 old tuberculin, with a poor result after twenty-two injections. The lowest dose was 0.3 cc. of 1:10,000 old tuberculin, with no improvement after fourteen injections. The best result followed twenty-one injections to a maxium dose of 0.75 cc. of 1:10,000 old tuberculin.

3. Van Studdiford, M. T.: Diagnostic and Therapeutic Use of Tuberculin in Certain Acneform Eruptions, Arch. Dermat. & Syph. **38**:737 (Nov.) 1938.

RESULTS

The results were very disappointing. No definite improvement was seen except in 1 patient. This woman had started with numerous papules on the cheeks, chin and submaxillary region. At the end of three months, the lesions were few and small. There were no clinical features in this case suggesting any sort of tuberculosis of the skin.

SUMMARY

Treatment with tuberculin for three months was beneficial to only 1 of 11 patients (9.1 per cent) with acne.

185 North Wabash Avenue.

104 South Michigan Boulevard.

LIVER EXTRACT IN THE TREATMENT OF ACNE VULGARIS IN TUBERCULOUS PATIENTS

M. R. LICHTENSTEIN, M.D.
AND
A. W. STILLIANS, M.D.
CHICAGO

The dermatologist in attendance in a sanatorium for tuberculosis sees little tuberculosis of the skin. His chief occupation is caring for such cutaneous diseases as acne and seborrheic conditions of the scalp. These often seem to loom as large in the patient's eyes as their pulmonary affliction. During past years we have been impressed by the large percentage of patients with acne who have given a history of a decided exacerbation in the cutaneous disease a few months after entering the institution. Our only explanation of this fact is that they are kept on a fattening diet.

In treating acne in these patients we have been constrained to say nothing of dietary restriction and we often cannot ask them to use vigorous local measures because of their physical weakness.

Hoping that the treatment of acne by injection of boiled liver extract, as advocated by Marshall,[1] might benefit our patients doubly by clearing the acne and aiding in improvement of general health, we undertook a study of this treatment beginning on Dec. 2, 1939.

During the first part of our work we treated 28 patients, 27 with acne simplex and 1 with acne indurata of the face, neck and back. They were given 0.4 cc. of liver extract which had been boiled a half-hour. The injections were intramuscular and were given twice a week. Some received as few as nine injections and others as many as twenty-seven. Objective changes were noted by two independent observers, and to guard against suggestion we asked the patient: "You don't see any change in your acne, do you?" No other treatment was given, not even extra scrubbing or the use of hot compresses. Of the 28, only 4 were visibly benefited. Two who received twenty-four injections each were considerably improved; 1 who received twenty-two injections and

From the City of Chicago Municipal Tuberculosis Sanitarium.

1. Marshall, W.: Further Studies on the Therapy of Acne Vulgaris with Modified Liver Extract, J. Invest. Dermat. **2**:205, 1939.

another who was given twenty obtained only slight benefit. The last-mentioned one was not gaining against his pulmonary disease, and the first 3 were improving.

Results of Liver Therapy on Acne Vulgaris in Tuberculous Patients

Patient	Sex	Age	Number of Injections	General Condition	Benefit
1	F	24	8	Fair	Moderate
2	F	17	30	Good	Great
3	F	20	15	Fair	None
4	M	19	42	Good	Slight
5	M	21	7	Good	None
6	F	19	17	Fair	None
7	M	22	37	Fair	Great
8	F	20	20	Good	None
9	F	24	19	Fair	Slight
10	F	16	19	Good	None
11	F	21	38	Good	Moderate
12	F	17	6	Good	Moderate
13	F	33	26	Good	None
14	F	21	22	Fair	Moderate
15	M	17	22	Good	Great
16	M	22	13	Good	Great
17	F	18	21	Good	None
18	F	20	15	Good	None
19	F	14	14	Fair	Moderate
20	F	23	13	Good	None
21	F	22	13	Good	None
22	F	20	13	Good	Great
23	M	19	13	Fair	None
24	M	34	13	Fair	None
25	F	18	13	Fair	None
26	M	20	9	Good	None
27	F	24	9	Good	Slight
28	F	22	13	Good	Great
29	F	18	13	Poor	Moderate
30	M	19	41	Fair	Moderate
31	M	30	56	Good	Great
32	M	24	15	Good	Slight
33	F	42	16	Good	Great
34	F	15	16	Good	Moderate
35	F	24	18	Poor	Slight
36	F	27	10	Fair	Slight
37	M	34	24	Poor	Moderate
38	F	18	9	Good	None
39	M	36	8	Fair	None
40	M	38	16	Good	None
41	M	38	7	Good	None
42	M	20	22	Good	Slight
43	F	15	23	Good	Great
44	F	24	17	Good	Great
45	F	22	41	Good	Great
46	F	29	16	Fair	None
47	M	23	17	Good	None
48	F	21	11	Good	Slight
49	F	19	52	Good	Moderate
50	F	22	18	Good	None
51	F	21	30	Fair	None
52	F	38	10	Poor	Great
53	F	21	21	Good	Moderate
54	F	33	8	Good	None
55	F	19	13	Good	None
56	M	16	19	Poor	None
57	F	24	11	Poor	None

This experience and the improvement in the material, a fraction obtained by Professor Farmer and Dr. Marshall from injectable liver extract (Abbott Laboratories), led us to begin the second part of the series in May 1940. The table gives the data for the whole series, from Dec. 2, 1940 to April 29, 1941. Fifty-seven patients were treated, most

of them with acne simplex or this with an occasional deep lesion and only 3 with real acne indurata of the face, neck and back. The dose of the new preparation was increased in most cases to 1 cc., given intramuscularly once a week.

The following results were obtained: 12, or 21.1 per cent, were greatly improved; 11, or 19.3 per cent, were moderately improved; 8, or 14 per cent, were slightly improved, and 26, or 45.6 per cent, received no benefit.

In no case was the condition made worse by the treatment.

Of 36 patients whose general condition was good and whose temperature was normal, 11 received great benefit from the treatment for acne, 5 were moderately helped, 5 received a little benefit and 15 failed to be benefited.

In the second group, those in fair general condition whose temperature was of low grade and loss of weight slight, there were 15. The skin of 1 was greatly improved; of 4, moderately improved, of 2, slightly improved, and of 8, not at all helped.

Of the 6 patients who were not responding to treatment for their pulmonary disease, who were losing weight and showing other signs of regression, 1 showed great improvement in the acne; 2 received moderate benefit; 1 was slightly improved, and 2 received no benefit.

The patients whose treatment was classed as failure were given an average number of fifteen injections. The patients who received slight benefit received on the average eighteen treatments. Those with moderate benefit received an average of twenty-three treatments each. The 12 who were greatly benefited had an average of twenty-four treatments.

One of the reasons for the lower average number of treatments for the patients who were not benefited is, of course, that they became discouraged and asked for a change of treatment or left the institution. Some of them who had received only seven to eleven treatments might have shown a different result if the treatment had been continued.

Few patients could be classed as benefited until they had received more than eleven injections.

Patients 7 and 13 (in the table) had acne indurata of the face, neck and back. They improved rapidly. A third patient with this condition did not improve and was given roentgen ray treatment. Patient 52 was in poor physical condition, losing ground in her battle for health, and in spite of this her acne cleared entirely under treatment with the liver extract.

This seems to us strong evidence against the view held by some that tuberculosis has some part in the causation of acne vulgaris. If, as some hold, acne is caused by excess of fat in the skin, it may have been some

interference with the absorption of fats that was responsible for the loss of weight and resistance as well as the cure of the acne.

We feel that our series has been a rather severe test of the liver extract method of treatment. Not only were we treating patients whose powers of resistance were lowered by disease but we were competing with a diet ideal for the promotion of acne vulgaris.

The chief objections to this treatment, if one judges from our results, are the following:

1. The results are slow in appearing. Most of those in our series who were benefited greatly had fairly prompt response in about two months. They constituted, however, only 21 per cent of our series. The slow response, if it holds good for nontuberculous patients, would necessitate using the injections as an auxiliary treatment combining with quicker methods, such as ultraviolet irradiation and application of lotions.

2. The percentage of good results is not high enough.

Both of these objections point to the necessity of combining other methods of treatment. We feel that we have demonstrated a definite action of the modified extract in certain cases of acne vulgaris in spite of a concomitant pulmonary tuberculosis.

SUMMARY

Fifty-seven patients with acne vulgaris and pulmonary tuberculosis were treated by injections of modified liver extract.

No other treatment for acne was given.

Twenty-one per cent of the patients were greatly improved; 19 per cent were moderately improved; 14 per cent were slightly improved, and 45 per cent received no benefit.

One patient received decided benefit in spite of progressive deterioration in her general condition.

185 North Wabash Avenue.

104 South Michigan Boulevard.

Clinical Notes

NATURAL COLOR LANTERN SLIDES

Description of Apparatus

THOMAS S. SAUNDERS, M.D., PORTLAND, ORE.

Dermatologists who use "view" or "clinical" cameras to make black and white photographs in the regulation (5 by 7 inch [12.8 by 17.8 cm.]) size may be interested in knowing that their cameras can be simply and quickly converted for making natural color lantern slides. A reducing back[1] with ground glass focusing, interchangeable with the 5 by 7 inch back, is available. A 2¼ by 3¼ inch (5.7 by 8.3 cm.) color film can then be exposed. Film holders of the graflex type are of course necessary. One large photoflood bulb on each side of and level with the camera will provide the necessary intense, flat lighting. The camera lens should be able to insure good color correction. The exposed film is processed without additional charge and is returned ready to be mounted in the regulation (3¼ by 4 inch [8.3 by 10.2 cm.]) lantern slide glass. The cost of the finished slide will be less than the charge made by the commercial finisher for black and white lantern slides. The reproduction of color on kodachrome film is excellent.

Medical Arts Building

1. Furnished by Burke and James, Chicago.

FOLLICULITIS OF THE CHIN WITH ENLARGEMENT RESEMBLING RHINOPHYMA

"Mentophyma"

TIMOTHY J. RIORDAN, M.D.; ORLANDO CAÑIZARES, M.D., AND GEORGE E. MORRIS, M.D., NEW YORK

Rhinophyma on rare occasions may be associated with enlargement of the forehead and chin. Sams[1] has reported the case of a woman with involvement of the chin simultaneous with rhinophyma. Stelwagon[2] stated that thickening of the chin sometimes occurs in cases of rosacea.

From the Department of Dermatology, New York University College of Medicine, and the Dermatological Service of the Third (New York University) Medical Division, Bellevue Hospital, service of Dr. Frank C. Combes.

1. Sams, W. M.: Rhinophyma with Unusual Involvement of the Chin, Arch. Dermat. & Syph. **26**:834 (Nov.) 1932.

2. Stelwagon, H. W.: A Treatise on Diseases of the Skin, ed. 9, Philadelphia, W. B. Saunders Company, 1921, p. 1115.

We have been unable to find enlargement of the chin reported as a distinct entity independent of rhinophyma. We suggest the name "mentophyma." In our case the hypertrophy followed long-standing sycosis vulgaris. No signs of rosacea had ever existed, and the nose was normal.

REPORT OF A CASE

M. D., a white man aged 46, was admitted to Bellevue Hospital with sycosis vulgaris. He stated that he had had this condition for twenty years, during which time he had been treated with different preparations but with little success. The enlargement of the chin had existed for four years.

Physical examination gave essentially normal results except for showing twenty-five or thirty scattered erythematous papules and pustules in the beard, especially on the chin. There were many pitted scars. The tip of the chin was hypertrophied and protruded about ½ inch (1.3 cm.). This mass was firm, lobulated and purplish. A considerable amount of sebaceous matter was expressed from the orifices. The nose was normal, and there was no evidence of rosacea.

Histologic examination showed essentially hyperplasia of the sebaceous glands together with hypertrophic hair follicles and a moderately diffuse lymphocytic infiltration. Microscopic examination of the hairs and cultures showed no fungi. The Wassermann reaction of the blood was negative. The urine and the blood count were normal.

The folliculitis improved with ordinary local therapy and the administration of sulfathiazole (2-[paraaminobenzenesulfonamido]-thiazole). The patient refused any cosmetic procedure.

SUMMARY

A case of "mentophyma" (folliculitis of the chin with enlargement resembling rhinophyma) without rosacea, following long-standing sycosis vulgaris, is reported.

136 East Sixty-Fourth Street.

601 West One Hundred and Thirteenth Street.

Bellevue Hospital.

CHLORHYDROXYQUINOLINE (QUINOLOR) OINTMENT IN THE TREATMENT OF ACNE NECROTICA MILIARIS OF THE SCALP

A. A. FISHER, M.D., WOODSIDE, N. Y.

Acne necrotica miliaris of the scalp is a fairly common disease which may cause intense suffering. Sabouraud[1] described it in 1928 under the title "acne necrotique miliaire." Lane[2] in 1933 reported the first cases in this country under the title "acne necrotica miliaris of the scalp." The disease which Ormsby[3] called "pustular perifolliculitis" is probably the same as acne necrotica miliaris of the

From the Department of Dermatology and Syphilology, Queens General Hospital, Jamaica, N. Y. (service of Dr. Ida Mintzer).

1. Sabouraud, R.: Pyodermites et eczémas, Paris, Masson & Cie, 1928, pp. 91-98.

2. Lane, J. E.: Acne Necrotica Miliaris of the Scalp, Arch. Dermat. & Syph. **28**:10 (July) 1933.

3. Ormsby, O. S.: Diseases of the Skin, ed. 5, Philadelphia, Lea & Febiger, 1937, p. 1210.

scalp. In 1937 Montgomery[4] reported 25 cases from the Mayo Clinic. McCarthy[5] agreed with the other authors that the histologic picture is that of acne necrotica of a minute type.

The patients whom I have observed have been seriously inconvenienced by the disease. They had tried numerous remedies without relief. The patients had suffered from localized areas of intense burning and itching of the scalp for a number of years. The commonest lesion was a pinhead-sized crust located about a hair. On several occasions a small pustule pierced by a hair was noted.

Prior to using chlorhydroxyquinoline (quinolor) ointment, I failed to obtain satisfactory results with any remedies that had been previously recommended. Since acne necrotica miliaris of the scalp is probably a staphylococcic infection, the use of quinolor ointment in the treatment of this disease seemed rational.

REPORT OF CASES

CASE 1.—Mrs. G. C., aged 33, complained of severe "itching pimples" of the scalp for three years. She had used sulfur ointment, ammoniated mercury and tar preparations without any relief.

Examination revealed six tiny dry crusts located about hairs. One tiny pustule surrounding a hair was seen. After the first application of quinolor ointment, relief was obtained. For the first time in three years no new lesions appeared. The use of the ointment once a week controlled the eruption satisfactorily. A concomitant neurodermatitis of the nuchal area cleared spontaneously with the improvement of the scalp.

CASE 2.—Mrs. A. K., aged 32, suffered from pruritic "bumps" throughout her scalp almost continuously for six years. This was specially annoying just before her menstrual period.

Examination revealed nineteen tiny crusted areas scattered throughout the scalp. The patient was highly nervous and was convinced that she had an incurable disease of a malignant nature.

After three consecutive nightly applications of quinolor ointment the "bumps" no longer appeared. Weekly applications of the ointment since then have controlled the eruption. The patient had blond hair, which was not discolored by the treatment.

CASE 3.—Mrs. B. J., aged 40, had consulted numerous specialists in the past six years because of severe itching of the scalp. She had obtained partial relief from the use of 10 per cent ammoniated mercury ointment.

Examination revealed thirty-seven pinhead-sized lesions scattered throughout the scalp. Examination with a hand lens revealed several tiny vesicopustules, giving the appearance of sycosis vulgaris. The other lesions were tiny crusts.

The use of quinolor ointment nightly for one week and thereafter once a week has satisfactorily controlled the eruption. The patient had red hair, which was not discolored by the ointment.

CASE 4.—Mr. K. C., aged 34, complained of burning and itching of the scalp of four years' duration. He had tried numerous proprietary remedies without relief.

Examination on several occasions usually revealed three or four small pinhead-sized crusted areas. There was premature baldness but no dandruff.

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4. Montgomery, H.: Acne Necrotica Miliaris of the Scalp, Arch. Dermat. & Syph. **36**:40 (July) 1937.

5. McCarthy, L.: Diseases of the Hair, St. Louis, C. V. Mosby Company, 1940, p. 285.

SUMMARY

In my 4 patients who have been followed for more than one year, the use of quinolor ointment quickly cleared the eruption. Its continued use once a week prevented recurrences. The itching and burning of the scalp disappeared after one or two applications. The ointment was usually rubbed into the scalp at night and washed out in the morning. It was used on a patient with blond hair and on one with red hair without causing any discoloration.

CONCLUSIONS

1. Acne necrotica miliaris of the scalp is a fairly common disease which may cause great distress and inconvenience.

2. The treatment advocated in the literature has not been efficacious.

3. The use of quinolor ointment on 4 patients who have been followed over a year has been most satisfactory.

45-14 Forty-Eighth Street.

Abstracts from Current Literature

EDITED BY DR. HERBERT RATTNER

THE WATERHOUSE-FRIDERICHSEN SYNDROME. JOHN A. MONTFORT and J. H. MEHRLING, Am. J. Dis. Child. **62**:143 (July) 1941.

This syndrome may be described as a fulminating purpura in association with bilateral adrenal hemorrhages. Meningococcemia is present in 60 per cent of the cases. Less commonly hemolytic streptococci are found and rarely pneumococci. The course is unbelievably rapid, and death may take place in from four to forty-eight hours after the onset. The diagnosis must be suspected shortly after the onset if any therapy is to be tried. Chemotherapy with the newer therapeutic agents, particularly those of the sulfanilamide group may be tried.

TULAREMIA WITH EXTENSIVE PHARYNGITIS. ROBERT R. ANSCHUETZ, Am. J. Dis. Child. **62**:150 (July) 1941.

This is the report of a case of tularemia in which the chief clinical manifestation of the disease was a necrotizing ulceration of the entire pharyngeal wall, extending to the surface of the tongue and to the oral mucosa. The author believes that this ulceration represents the point of entry of the organisms into the body. He refers to 3 similar cases in the literature.

NELSON PAUL ANDERSON, Los Angeles.

THE VIABILITY OF THE SPIROCHETES OF SYPHILIS AND YAWS IN DESICCATED BLOOD SERUM. THOMAS B. TURNER, JOHANNES H. BAUER and FRED C. KLUTH, Am. J. M. Sc. **202**:416 (Sept.) 1941.

There is an increasing number of transfusions with refrigerated whole blood and with blood serum or plasma which has been stored in the liquid or desiccated state. Previous studies had suggested that it is probable that blood stored for four days or longer, even though taken from a syphilitic donor, could no longer transmit this disease. The present report concludes that the transfusion of desiccated blood serum or plasma is probably without risk as regards the transmission of syphilis even though the material be obtained from an infected donor. The experiemental studies were conducted with frozen and desiccated material from infected rabbits.

LYNCH, St. Paul.

THE SYNDROME OF MILIAN'S ERYTHEMA OF THE NINTH DAY. E. E. PETERS, Am. J. Syph., Gonor. & Ven. Dis. **25**:527 (Sept.) 1941.

Fifty-four patients with the ninth day erythema of Milian syndrome are reported. Fifty-two had cutaneous manifestations, and 2 did not. The drugs producing this condition were arsphenamine, neoarsphenamine, mapharsen and acetylglycarsenobenzene. The eruption appeared between the seventh and the twentieth days after the first injection, and the majority of patients were acutely ill. Associated visceral reactions occurred in 24 per cent of this series. Further treatment with the arsphenamine drugs produced delayed complications in 53 per cent of 36 patients, and 70 per cent of all patients receiving further arsenical preparations had reactions.

Erythema of the ninth day is a generalized, systemic, self-limited reaction of which the cutaneous phenomenon is but one of many manifestations. The exact mechanism of the production of this condition is unknown. However, it is not specifically related to infection with Spirochaeta pallida, since it occurs in non-

syphilitic patients. The identical symptom complex may be produced with drugs other than the arsphenamine compounds.

The further administration of arsenical drugs should be withheld for at least one month after recovery from the reaction and then resumed cautiously with small doses.

THE DEVELOPMENT OF GENERAL PARESIS FOLLOWING ESSENTIALLY NORMAL SPINAL FLUID FINDINGS. I. KOPP and H. C. SOLOMON, Am. J. Syph., Gonor. & Ven. Dis. **25**:583 (Sept.) 1941.

The authors tabulate the clinical, serologic and therapeutic course of a patient with early minimal involvement of the spinal fluid from the onset of the syphilitic infection to the time of development of dementia paralytica. Fourteen months after the primary lesion the spinal fluid of the patient revealed minimal changes, and twenty-two months later it was essentially normal. Nevertheless, despite fairly continuous antisyphilitic therapy for fourteen years parenchymatous neurosyphilis developed, the patient presenting the characteristic mental symptoms of dementia paralytica as well as changes in the spinal fluid typical of this condition.

AUTOHEMOTHERAPY IN CASES OF FIXED SEROLOGIC REACTIONS WITH NEGATIVE RESULTS. I. KOPP and H. C. SOLOMON, Am. J. Syph., Gonor. & Ven. Dis. **25**:591 (Sept.) 1941.

Persistently positive reactions to Wassermann and flocculation tests of the blood are commonly obtained in cases of neurosyphilis despite treatment which has been adequate in reversing the serologic reactions of the spinal fluid and maintaining them so.

Despite previous favorable reports regarding reversal of the serologic reactions of the blood, the authors found autohemotherapy to have no therapeutic effect of reversing a "Hinton-fast" reaction of the blood.

SHORT TERM INTENSIVE ARSENOTHERAPY OF EARLY SYPHILIS. A. SCHOCH and L. J. ALEXANDER, Am. J. Syph., Gonor. & Ven. Dis. **25**:607 (Sept.) 1941.

Twenty-nine patients with primary and secondary syphilis have been treated with daily injections of mapharsen, the original plan of giving a full therapeutic dose each day for twenty days having been modified to giving two full therapeutic doses one-half hour apart daily for ten days. No reactions to the treatment were encountered that necessitated interruption or discontinuance of therapy.

To date, seven months or longer after treatment, 26 patients are clinically and serologically well. Of this group 1 patient had a clinical relapse and 1 a reinfection; they were retreated and are now clinically and serologically well. Two patients sustained serologic relapse, and another gives a positive reaction to a Kline test only.

RARE OCULAR REACTIONS TO TRYPARSAMIDE. S. E. C. TURVEY, Am. J. Syph., Gonor. & Ven. Dis. **25**:623 (Sept.) 1941.

Thirteen cases are reported in which late ocular reactions to tryparsamide occurred. These reactions occurred after injections 20, 78, 37, 55, 16, 42, 35, 14, 45, 18, 23, 52 and 33 respectively. The assumption that all ocular reactions occur before the tenth injection is unwarranted and unsafe. REUTER, Milwaukee.

ACROPACHYDERMA WITH PACHYPERIOSTITIS. HEINRICH G. BRUGSCH, Arch. Int. Med. **68**:687 (Oct.) 1941.

Brugsch describes a condition and reports a case of a disturbance in growth characterized by clubbing and squaring of the extremities, thickening of the skin on the face, scalp and extremities and deformities of the long bones and their periost. The thickening and furrowing of the skin resemble the condition known

as cutis verticis gyrata, which has occasionally been described in association with enlargement of the hands and feet. In Brugsch's case histologic examination of the skin revealed hypertrophy of certain parts, mainly of the corium, sweat glands and oil glands. The face appeared fatty, and the openings of enlarged sebaceous glands were evident.

LYNCH, St. Paul.

THE FATE OF TREPONEMA PALLIDUM INOCULATED SUBCUTANEOUSLY INTO IMMUNE RABBITS. FRANK W. REYNOLDS, Bull. Johns Hopkins Hosp. **69**:53 (July) 1941.

If an animal, such as the rabbit, susceptible to syphilis is inoculated with Spirochaeta pallida there develops an active immunity. This immunity eventually becomes sufficiently strong not only to heal all manifest lesions of the disease but to render the animal resistant to reinfection, especially with homologous strains of spirochetes. Further, once this immune state is fully developed, it is not dissipated by treatment with spirocheticidal drugs. Whether or not this persistence of immunity after treatment is due to survival of the original infection (e. g., an infection immunity) is disputed. Nevertheless, virulent spirochetes of homologous strains fail to produce visible lesions when inoculated into animals which have been treated in the late stages of the disease (e. g., after the development of an immune state). Reynolds did experimental work to ascertain the ultimate fate of these spirochetes. Does a "symptomless reinfection" occur by permeation of the tissues of the host, or are they destroyed by the immune mechanism of the host? He ascertained that such spirochetes do not migrate to the regional lymph glands but are immobilized and destroyed in situ by the immune processes of the host.

NELSON PAUL ANDERSON, Los Angeles.

THE FIVE-DAY TREATMENT OF SYPHILIS. HERBERT RATTNER, Illinois M. J. **81**:29 (Jan.) 1942.

Since August 1940 the author has treated 170 patients with early syphilis by means of the intensive intravenous drip method with mapharsen. Clinical results are reported for the first 80 patients, 14 of whom have been dropped from the study. Relapses have occurred in 3 patients and probably in a fourth. Two patients had reinfections and 2 others possible superinfections. In 6 others the results were considered "unsatisfactory when last seen." In 6 patients treated during the seronegative primary stage of syphilis, the blood tests give persistently negative reactions; all of the patients with relapses had been treated originally for an eruption of secondary syphilis. Reactions included hemorrhagic encephalitis in 1 case and a single convulsion in another. Minor reactions were phlebitic pain in the arm, nausea, emesis and slight headache. No cases of exfoliative dermatitis, hepatic or renal damage, blood dyscrasia, embolus or nitritoid reactions were encountered. There have been no fatalities at the Cook County Hospital from this method of treatment.

The author concludes that the method shows great promise but still must be considered in the experimental stage. However, it seems likely that the introduction of the intensive intravenous drip method of treatment may well prove to be the most significant advance in the treatment of syphilis since the introduction of arsenic.

BLUEFARB, Chicago.

THE ROENTGEN RADIATION OF PAPILLOMA VIRUS (SHOPE): II. THE EFFECT OF X-RAYS UPON PAPILLOMA VIRUS IN VITRO. J. T. SYVERTON, G. P. BERRY and S. L. WARREN, J. Exper. Med. **74**:223 (Sept.) 1941.

A great deal of interesting experimental work is being performed with viruses, papillomas in rabbits and the cancers which often result from these growths. The present report is concerned with the effect of radiation on cell-free suspensions of the Shope papilloma virus. The study shows that complete inactivation of this

virus requires tremendous doses (millions of roentgen units), more than is required to inactivate other infectious agents which have been studied and more than the doses required to cause regression of the tumors caused by the virus.

LYNCH, St. Paul.

REGIONAL, RACIAL, AND FAMILIAL RELATIONSHIPS IN LEPROSY IN THE UNITED STATES. W. L. AYCOCK and J. W. HAWKINS, Pub. Health Rep. **56**:1324 (June 27) 1941.

The prevalence of leprosy in certain areas in the United States appears to be dependent in part on the presence of cases as sources of infection and in part on the presence in these areas of certain racial stocks or families.

The regional, racial and familial relation in certain of the persons of German descent with the disease suggest a further study of familial occurrence in this and other racial groups within the United States.

A NEW INDUSTRIAL SKIN CLEANSER. L. SCHWARTZ, Pub. Health Rep. **56**:1788 (Sept. 5) 1941.

For a good skin cleanser that will not defat the skin, the author recommends a mixture consisting of sulfonated castor oil having a p_H of 7.2 and an oil content of 50 per cent with 2 per cent of one of the wetting agents santomerse, duponol or igepon. The mixture is used in the same way as liquid soap; a drachm or 2 (4 to 7 cc.) is put in the palm and rubbed into the skin and then washed off with water. The cleansing properties of the mixture can be increased by adding an alkali, such as trisodium phosphate, 1 to 2 per cent, or sodium hexametaphosphate in the same proportion. The alkali, however, may impart a "sting" to the mixture. The use of this cleansing mixture has been very satisfactory in the author's experience.

DERMATITIS FROM CUTTING OILS. LOUIS SCHWARTZ, Pub. Health Rep. **56**:1947 (Oct. 3) 1941.

Cutting oils are the most frequent causes of dermatitis among machinists and metal workers. Cutting oils are divided into two large groups, the insoluble and the soluble. The soluble oils in general consist of mineral oil, soap and volatile matter and are used mainly as cooling agents. The insoluble oils consist principally of mineral oil, fatty oil, sulfur and chlorine and are used mainly as lubricants.

All petroleum oils have the property of defatting the skin. All oils may plug up pores of the skin and form comedos. The chlorine and sulfur content may irritate the skin. The animal or vegetable oils, especially when rancid, may irritate or sensitize the skin of some workers. Inhibitors, such as phenols, cresols and nitrobenzene, added to cutting oils to prevent rancidity, may act as sensitizers and cause allergic eczema.

Comedos, folliculitis, boils and carbuncles and infected wounds of the skin caused by metallic slivers are common in workers using cutting oils. Drying, fissuring and cracking of the skin often result from the defatting action of the oils. Allergic eczemas are caused by hypersensitivity to animal or vegetable oil, or inhibitor, but are rather infrequent. Mineral oils undoubtedly cause a few cases of cancer of the skin, but fortunately the mineral oils of North America are low in carcinogenic properties.

Prevention of dermatitis from cutting oils consists chiefly in cleanliness of the person, of the clothes, of the machines and of the oil. Protective ointments should be composed of animal or vegetable fat to prevent the entrance of the mineral oil into the pores of the skin.

THE TECHNIC OF INDUCED MALARIA AS USED IN THE SOUTH CAROLINA STATE HOSPITAL. BRUCE MAYNE and MARTIN D. YOUNG, Ven. Dis. Inform. **22**:271 (Aug.) 1941.

There are two primary methods of transferring malarial infection from one patient to another. The one widely used is the transfusion of blood from a malarious donor to the recipient. The second is through the bite of infected mosquitoes. This method requires the setting up of an insectary to breed the mosquitoes. Infected mosquitoes can be shipped successfully. Another method is the removal of infected salivary glands of the mosquito under aseptic conditions and placing the sporozoite material in sterile sodium citrate, which can be readily shipped.

Quartan malaria is the malaria of choice when time is not a factor. The intravenous route of injection of malarial blood or culture of sporozoites is routinely used by the authors. The number of paroxysms allowed usually is about twenty. While undergoing paroxysms, the patient is treated symptomatically. Sodium chloride is given routinely to replace some of the salts lost during the sweating period. The principle indications for termination of the infection are sudden overwhelming infection, severe anemia, unremitting pyrexia, extreme exhaustion, cyanosis, edema, renal disturbances, severe jaundice and marked increase in blood urea. Quinine is used routinely for termination of the infection.

Contraindications to treatment with induced malaria are the presence of any chronic infectious disease, cardiovascular or renal disease, severe emaciation, acute and rapidly developing dementia paralytica, severe anemia, hepatic dysfunction, senility and extreme obesity.

THE INDICATIONS FOR THERAPEUTIC MALARIA IN THE VARIOUS FORMS OF NEUROSYPHILIS. JOSEF GERSTMANN, Ven. Dis. Inform. **22**:277 (Aug.) 1941.

Malarial therapy is the treatment of choice for parenchymatous neurosyphilis and especially dementia paralytica. In cases of tabes dorsalis malarial therapy should be used only if the usual specific treatment together with milder nonspecific methods, such as the use of old tuberculin, typhoid vaccine and other pyretogenic substances, has been ineffective. In cases of primary atrophy of the optic nerve the best results are to be obtained with inoculation malaria therapy in modified form. For interstitial or meningovascular neurosyphilis, malarial therapy should be used only if other methods fail. For asymptomatic neurosyphilis, the use of malarial therapy with supplementary chemotherapy is the method of choice, and there is ample evidence to show that with this form of therapy the development of late parenchymatous neurosyphilis may be prevented.

ANALYSIS OF 532 CASES OF INTERSTITIAL KERATITIS WITH PARTICULAR REFERENCE TO STANDARDIZATION OF TREATMENT. J. V. KLAUDER and E. VANDOREN, Ven. Dis. Inform. **22**:307 (Sept.) 1941.

A report is made of an analysis of 532 patients with interstitial keratitis who were treated or observed for at least one year. The median age at the onset was 12 years for females and 13 years for males. Two and five-tenths per cent of patients with active interstitial keratitis who were untreated had a negative serologic reaction of blood.

The following scheme of treatment is recommended on the basis of the present study and the experience of the authors: Fever therapy should be employed as soon after onset as possible. Because arsenicals and bismuth are antimalarial, their use should be withheld during the course of induced malaria, but they should be given in the interval between fever bouts produced by other agents. Treatment should be continuous throughout the active stage of the disease and should consist of approximately thirty injections of an arsenical and sixty of a bismuth compound. The administration of iodides is not recommended.

REUTER, Milwaukee.

ENDOCRINE FACTORS IN ACNE VULGARIS. E. LIPMAN COHEN, Brit. J. Dermat. **53**:231 (Aug.-Sept.); 269 (Oct.) 1941.

In two articles the author has given an exhaustive survey of the role that the endocrine glands have played in regard to causation and treatment of acne vulgaris. The strongest arguments in favor of an endocrine causation are the regularity of the appearance of the disorder at puberty and its variation with the menses. Acne occurs with abnormal frequency in conjunction with certain diseases of the endocrine system, such as tumors of the adrenal cortex and arrhenoblastomas, and also during the administration of androgens, such as testosterone propionate. Apart from these, it does not occur regularly with the major endocrine disorders. Particular confusion exists with regard to the results of treatment. It appears that in those cases in which some disease of the endocrine system is clearly present, the treatment of that disease will also improve the acne; beyond that it is as yet impossible to draw final conclusions.

MOLLUSCUM CONTAGIOSUM AND M. & B. 693. JAMES SOMMERVILLE, Brit. J. Dermat. **53**:255 (Aug.-Sept.) 1941.

Eight patients with molluscum contagiosum were treated with sulfapyridine (2-[paraaminobenzenesulfonamido]-pyridine). In 6 of these the disorder cleared up completely, and in the cases of the other 2 treatment was suspended early owing to toxic upset. The author does not suggest that this treatment should replace the easy and convenient local measures already in use but presents this report to show that sulfapyridine has a definite lethal effect on the causative virus of molluscum contagiosum.

A POSSIBLE CASE OF KAPOSI'S SARCOMA. A. A. MCINTOSH NICOL and H. A. COOKSON, Brit. J. Dermat. **53**:283 (Oct.) 1941.

The authors report a case of sarcoma of the skin which appeared to possess some of the clinical and histologic features of Kaposi's sarcoma. A postmortem examination was not made.

BLUEFARB, Chicago.

PINK DISEASE TREATED BY INTRAMUSCULAR VITAMIN B_1: A REPORT OF EIGHT CASES. JOHN DUNCAN HAY, Practitioner **146**:264 (April) 1941.

A study of this series suggests that in some cases pink disease may respond to intramuscular thiamine (vitamin B_1) therapy but that such a result must not be expected in all. Such a finding can be satisfactorily explained only by a knowledge of the cause of the condition, which is not at present available. On the vitamin deficiency theory, it may be suggested that in cases in which there is no response to treatment enough vitamin has not been given; or, alternately, that changes have taken place in the tissues which are, at any rate temporarily, irreversible, or, finally, that secondary infection, such as Vincent's infection of the mouth, is interfering with the action of the vitamin. On the infective theory, the successes of vitamin therapy may be attributed to its ability to raise the resistance of the body to the infection, especially in the cardiovascular and nervous system; and the failures, to the presence of an infection too severe to be dislodged by an increase in bodily resistance alone.

Whatever may be the true explanation of the part thiamine plays in this interesting disease, it would seem wise to continue to administer it intramuscularly in the hope of relieving some patients and of preventing the disease from becoming severe in others. It would also seem advisable to give the other fractions of vitamin B. By this treatment one not only would be adopting the only method which at present appears able in some instances to cause marked improvement but would, in addition, be providing further material on which to base a more accurate knowledge of the role of vitamin B deficiency in the causation of the disease.

AUTHOR'S SUMMARY. [AM. J. DIS. CHILD.]

GIANT SYPHILOID GRANULOMA ANNULARE. J. CAPURRO and A. BIGATTI, Bol. Soc. de dermat. y sif. **6**:74 (March 13) 1941.

The authors describe a case of granuloma annulare of eight years' duration. The lesions appeared on the distal third of the arms and legs. The plaques were oval and 3 to 4 inches (7.5 to 10 cm.) in diameter. The centers of the lesions were smooth and pink. The borders were formed by numerous inflammatory papules, 2 to 3 mm. in diameter. In some of the lesions the ring was not entirely closed. The Wassermann reaction of the blood was negative. The reaction to a tuberculin test was weakly positive. Therapeutic test with the arsenicals failed to improve the lesions. Histologic examination showed chronic granuloma suggestive of granuloma annulare.

THE INTRADERMAL TEST OF MONTENEGRO IN LEISHMANIASIS. LUIS DE SALLES GOMES, Brasil-med. **53**:1079 (Dec. 2) 1939.

In 1926 Montenegro introduced an intradermal test as an aid in the diagnosis of leishmaniasis. The antigen used was a suspension of washed flagellates in physiologic solution of sodium chloride.

Of 120 cases, in 97.5 per cent the test elicited strong or moderate reactions and in 2.5 per cent weak reactions. An antigen eighteen months old also elicited strong reactions. The intravenous injection of the antigen elicited an allergic shock which was parallel to the intensity of the cutaneous reaction. Different species of leishmania bodies gave similar results, showing that the reaction was a group reaction. The test gave negative results in control cases, including instances of American trypanosomiasis.

THE LEPRA REACTION. ERNESTO ESCALONA, Prensa méd. mex. **6**:127 (Sept. 15) 1941.

The author makes a complete study of the acute manifestations of lepra, called also "lepra reaction," "lepra fever" and "acute leprous attack." He has observed numerous reactions of this type in patients in Zoquipara Leprosarium. This acute manifestation is so frequent that it may be said that all the patients have had it with more or less intensity.

The typical manifestations of the "lepra reaction" are chills, malaise and pain in the joints and muscles. In some cases there is a painful adenitis, generalized or localized.

These symptoms precede the more definite cutaneous or nervous manifestations. The cutaneous lesions are of different types. The erysipelas-like type may be localized on the face or legs. The peculiarity of this type is its wandering character. The erythema multiforme type, usually of the papular form, is frequently observed. Erythema nodosum is observed not only on the legs but also on the arms and face. The nervous manifestations are observed along the peripheral nerves, which become very painful and enlarged.

Laboratory examinations help in making a diagnosis. There is a leukocytosis. The sedimentation rate is of prognostic value. Hansen's bacillus is abundant in the cutaneous lesions and in the lymph nodes.

There are atypical forms which may resemble typhoid fever; others are very persistent and may be present for months. There are two special types of lepra reaction which deserve special attention: one is the tuberculoid form and the other the macular type of Lucio. The former is usually noticed in cases of the tuberculoid form of leprosy but may be seen with other forms. The lesions already present may become congested, and a halo appears about them. Later, larger, dark red, smooth plaques are apparent. This tuberculoid reaction is seen also in the nerves. The causative organism is easily found in the lesion, in contrast with its scarcity in the tuberculoid type not during "lepra fever." The macular type of Lucio is characterized by small macules which turn purpuric and later become

ulcerated. The cutaneous lesions are always associated with systemic manifestations.

The treatment is symptomatic. Calcium gluconate and fuadin seem to be effective. Adrenal extracts are used during the period of convalescence.

TESTICULAR LESIONS IN LEPROSY. R. BARRERA TENORIO, Prensa méd. mex. **6**:130 (Sept. 15) 1941.

The author made a study of the testicular lesions of 100 patients with leprosy. In some instances the lesions on the penis resembled a syphilitic chancre, and in some cases even inguinal adenitis was present. The genital lesions in leprosy are frequent and appear early. Of the 100 patients examined, 70 presented such lesions; 55 of them had leproma, and 15 had nervous lesions. Orchiepididymitis due to the leprosy bacillus leads to atrophy, and the patient becomes impotent.

The lesions are usually bilateral and may be smooth or nodular. It was observed that patients who became infected before puberty failed to show the secondary sexual characteristics. The genitals were of infected type; the hair of the axillas and pubis was scant, and the sexual instinct was absent. In patients who contracted the disease soon after puberty there was an increase in the sexual activities with gradual diminution later.

COURSE AND PROGNOSIS OF TUBERCULOID LEPROSY. S. SCHUJMAN, Rev. brasil. de leprol. **7**:1 (March) 1939.

The author states that he has never found a report of a proved case of tuberculoid leprosy changing into the lepromatous type. Clinically the differential diagnosis between a tuberculoid lepra reaction and lepromatous lesions is difficult. The diagnosis is helped by the Mitsuda cutaneous test, which always elicits a positive reaction in tuberculoid conditions. Later observation of the case will be decisive: a tuberculoid lepra reaction will subside in a few months, while lepromatous lesions will continue to progress.

Having observed 100 cases of tuberculoid leprosy, many of them followed from seven to ten years, the author concludes that tuberculoid leprosy does not change into the lepromatous type. In answer to a questionnaire sent by the author, many authorities, including Darier, Gougerot, Fidenza and Fernandez, agreed with him. He considers the tuberculoid leprosy as a special allergic form of the disease with a positive Mitsuda reaction and good prognosis, as opposed to the lepromatous type, or anergic type, with a negative Mitsuda reaction and bad prognosis.

A NEW TEST FOR THE DIFFERENTIAL DIAGNOSIS BETWEEN SYRINGOMYELIA AND NEURAL LEPROSY. SALOMON SCHUJMAN, Rev. brasil. de leprol. **7**:405 (Dec.) 1939.

The author used for the first time the intradermal injection of histamine to differentiate between syringomyelia and lesions of neural leprosy. It produced the triple response when injected in anesthetic patches of the skin in cases of syringomyelia but failed to produce this reaction when injected in similar patches in cases of leprosy. The peripheral neuritis of leprosy suppresses the pathway of the axon reflex. In syringomyelia and other conditions of anesthesia of central origin the cutaneous nerves are intact and the histamine flare may therefore be produced.

IMPORTANCE OF THE ANORECTAL EXAMINATION IN THE CAMPAIGN AGAINST VENEREAL DISEASES. JACOB LERNER, Rev. chilena de hig. y med. prev. **3**:247 (March) 1941.

In a study of 73 cases of suspected anorectal involvement, in 41 per cent of the instances pathologic changes were found. In many patients the disease started with symptoms suggestive of dysentery. In early lymphogranuloma venereum of the rectum the author has frequently found vegetations and skin tags of varying

size. A chancroidal ulcer if undiagnosed may become depressed and surrounded by condyloma-like lesions. This condition might be confused with hemorrhoids. Perverted sexual intercourse was confessed by 26 per cent of the patients examined and by 63 per cent of those with anorectal manifestations. In 1 case there was an association of gonococcic proctitis with rectal lymphogranuloma venereum.

Possible Transplancental Transmission of the Virus of Lymphogranuloma Venereum. Olga Monetta O. and Waldemar E. Coutts, Rev. chilena de hig. y med. prev. **3**:257 (March) 1941.

There are several reports of pregnancy and delivery in cases of active lymphogranuloma venereum. The authors review the literature on the subject. In a careful study of the 3 cases they were unable to find any evidence of prenatal infection. Granulocorpuscles of Miwagawa were not found, and microscopic examination of the placenta and cord failed to show evidence of pathologic changes. The Frei test of the infants gave negative results.

Experimental Studies on Leishmaniasis. Hernando Rey-Matiz, Rev. Fac. de med., Bogotá **10**:52 (July) 1941.

Cutaneous leishmaniasis is frequently observed in Colombia. Material obtained from 2 cases in which the organism was found was injected intradermally in 2 dogs. Twelve days later a nodule appeared at the site of the inoculation, which later ulcerated and exuded pus. A second inoculation in another dog gave the same results. The causative organism was found in abundance in the lesions produced experimentally.

Cañizares, New York.

Adiponecrosis and Cold. H. Haxthausen, Nord. med. **27**:1174, 1940.

According to H. Haxthausen, severe cold can cause a peculiar indurated infiltration of the subcutaneous fatty tissue of the face (cheeks and chin), especially in small children. Histologically there is necrosis of the fatty tissue accompanied by inflammatory reaction, with lymphocytes in the supporting tissue of the fatty layer and a few lipoblasts—the latter being evidence of the regeneration process. The condition develops within a few days of severe exposure. Although the symptoms differ from those of frostbite and chilblains, the latter may both occur in addition to the necrosis. Clinically as well as histologically the picture resembles that of so-called adiponecrosis neonatorum, which may be brought about by mechanical trauma at birth. In either case the necrosis of the fatty tissue is seen in very early life; in later years the tissues seem to be able to withstand cold and trauma better. The prognosis is favorable. In cases reported by the author there was spontaneous remission within a few weeks.

Abt, Chicago. [Am. J. Dis. Child.]

Society Transactions

MANHATTAN DERMATOLOGIC SOCIETY

DAVID L. SATENSTEIN, M.D., *President*

ANTHONY C. CIPOLLARO, M.D., *Secretary*

Nov. 11, 1941

Darier's Disease. Presented by DR. E. WILLIAM ABRAMOWITZ.

F. G., a woman aged 30, a dental assistant, was presented by Dr. Howard Fox before this society on April 12, 1938 (ARCH. DERMAT. & SYPH. **38**:654 [Oct.] 1938). At that time, though it was not stated in the history, she also had lesions on the hard palate and gums.

She appeared at my office on July 3, 1941 and was given 100,000 U. S. P. units of vitamin A daily. She has taken the vitamin regularly with slight interruptions since then.

All lesions have shown considerable regression except those on the palms and soles. The lesions in the mouth have also improved.

DISCUSSION

DR. SAMUEL PECK: There seems to be no doubt that this patient has improved under vitamin A therapy. It would interest me to know whether there was a recurrence of the lesions during the summer months, in spite of the large doses of vitamin A. In a number of my patients with Darier's disease who had improved substantially when given from 150,000 to 200,000 U. S. P. units of vitamin A during the winter months, there seemed to be some recurrence of the disease during the summer months. The character of the recurrence was somewhat different. It was more inflammatory and was usually present on surfaces which were especially prone to maceration and hyperhidrosis. Such areas were the axillas in males and females and the skin between and under the breasts in females. Patients in whom vitamin A therapy had been discontinued after improvement or even complete involution of the original lesion showed a recurrence which was limited, as far as I could judge, to the sites of previous lesions. It was also possible to produce what could be described as an acute bullous type of Darier's disease by an overdose of vitamin A, usually above 300,000 U. S. P. units daily. I am at present puzzled to observe that when vitamin A is given in sufficient dosage intramuscularly, instead of the vitamin A content of the blood increasing, it actually decreases. In one patient who received 500,000 U. S. P. units intramuscularly in one week, vitamin A practically vanished from the blood stream.

DR. DAVID BLOOM: Has Dr. Peck followed my suggestion in regard to determination of the vitamin A status in other members of the families of patients with Darier's disease? The number of members affected is smaller than one would expect in dominant inheritance. This means that the cutaneous disease is not expressed in 100 per cent of those having the predisposition. It is possible, however, that in these members the morbid genetic factor will be manifested not in cutaneous changes but in changes in vitamin A metabolism.

DR. JACK WOLF (by invitation): Dr. Wise and I saw this patient several years ago and made a diagnosis of Darier's disease at that time. She was seen by another physician prior to that, who performed a biopsy which substantiated the diagnosis. The patient received grenz ray therapy without effect. At that time vitamin A had not yet been introduced for the treatment of Darier's disease.

DR. PAUL E. BECHET: If further investigation will prove that keratosis follicularis is definitely due to vitamin A deficiency and that the administration of vitamin A will cause its disappearance, a great step forward will have been taken in dermatotherapy. The course of Darier's disease has hitherto been progressive, and while radiotherapy has proved beneficial, it has never resulted in a permanent cure.

DR. HERMAN SHARLIT: I should like to know whether the patients get well enough so that they may maintain their improvement without further need for therapy.

DR. SAMUEL PECK: Six of the patients with Darier's disease were allowed to discontinue their vitamin A treatment over the summer months. Four of them had recurrences, which were not as extensive as the eruptions presented before the initiation of vitamin A therapy. Apparently, because of the rather large doses of vitamin A the patients received, enough of a depot resulted which prevented more extensive recurrences.

DR. E. WILLIAM ABRAMOWITZ: The patient had a recurrence during the summer. Her tonsils had to be removed, so she was advised to discontinue the vitamin A therapy during that period. Since the vitamin A treatment has been resumed the lesions on the trunk have almost disappeared. Those on the palms and soles and in the mouth are still noticeable. The lesions on the palms and soles regressed much slower than those in other areas.

The literature on excessive vitamin A dosage only cites examples of ill effects in animals. Some animals even died, but as far as I know nothing like this has happened in man. This woman has received 150,000 U. S. P. units a day. Tonight she complained of being irritable and nervous; so I told her to reduce the dose to 75,000 units. Of course the capsules contain not only the natural vitamin A but also vitamin D. Therefore, some effects may be produced by the vitamin D.

Epidermolysis Bullosa; Supernumerary Auricle. Presented by DR. DAVID BLOOM.

P. E., a girl aged 7 months, came to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Oct. 6, 1941 with an eruption on the hands and feet which had been present since birth.

The past history and family history were entirely irrelevant, according to statements by the mother.

On examination there are a few flaccid and broken bullae and scaly collarets, the remnants of bullae. On the right side of the neck there is a skin-colored nipple-like tumor, ½ inch (1.3 cm.) long, which on palpation reveals a firm cartilaginous core extending into the underlying tissue.

DISCUSSION

DR. MAURICE J. COSTELLO: Some one questioned the fact that there is a cartilaginous core in a lesion of this kind. I reported a number of cases of supranumerary rudimentary auricles, and clinically and histologically there is a cartilaginous core in the center of the lesion. The condition is often associated with other congenital abnormalities, such as supranumerary nipples, and has a familial tendency.

Linear Papular Pigmented Nevus; Supranumerary Auricle; Ptosis of the Eyelid. Presented by DR. DAVID BLOOM.

C. D., a Negro boy aged 6½ years, came to the dermatologic clinic of Sydenham Hospital complaining of a lesion on a finger which had been present since birth.

On the palmar aspect of the third and second phalanx of the right ring finger, somewhat more to the radial side, there is a line of hyperpigmented, slightly raised, pinpoint-sized to pinhead-sized papules.

On the left side of the neck there is a skin-colored nipple-shaped lesion which on palpation reveals a hard cartilaginous-like core, ¾ to 1 inch (2 to 2.5 cm.) long, which is attached to the deep tissues.

The child also has ptosis of the left eyelid, which, like the other anomalies, has been present since birth.

Of the three anomalies, only ptosis is present in the father.

Granuloma Annulare. Presented by Dr. David Bloom.

L. P., a girl aged 3 years, came to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Aug. 25, 1941, complaining of an eruption of one and a half years' duration. The past and family history were irrelevant.

On the dorsum of the left foot, on both knees and legs and on the dorsum of the left hand there are quarter-sized to dollar-sized, round, slightly erythematous plaques with clearing centers and raised borders. On the buttocks and posterior aspects of the thighs there are numerous dime-sized to quarter-sized, slightly erythematous plaques, some of which show a distinctly raised border. The eruption is not associated with any subjective symptoms.

General examination of the child did not reveal any abnormality. The result of a tuberculin test with a 1:10,000 dilution was negative.

The patient received two exposures of ¾ skin unit (225 r) of unfiltered roentgen rays to the dorsum of the left hand and to the right knee with slightly beneficial effect.

DISCUSSION

Dr. E. William Abramowitz: Was the urine examined? A few years ago I observed a child who had a typical granuloma annulare while the mother presented a typical example of necrobiosis diabeticorum. Clinically this condition looks like granuloma annulare, but I should not take it entirely for granted unless it was confirmed by histologic study.

Dr. S. Peck: This patient presents the type of granuloma annulare which can easily be confused with necrobiosis. Cases of this kind were shown at the meeting of the American Academy of Dermatology and Syphilology in Chicago.

Dr. Paul E. Bechet: Despite what has been said to the contrary, I still believe that the lesion is granuloma annulare.

Dr. Isadore Rosen: I wonder whether it might not be a good plan for the pathologists to review some of their slides, check on the number of cases of granuloma annulare that have been presented at the various meetings and note changes that suggest necrobiosis. Conditions like this and others resembling it clinically which were presented as examples of granuloma annulare may really have been necrobiosis.

Dr. Wilbert Sachs: The case (Dr. Miller's) referred to by Dr. Abramowitz was a typical one of necrobiosis lipoidica. Both Dr. Satenstein and I made the diagnosis with the ordinary hematoxylin-eosin stain. While occasionally granuloma annulare and necrobiosis lipoidica simulate each other microscopically, usually there is little difficulty in differentiating them. I do not think it makes much difference whether or not the patient had diabetes.

Dr. Fred Wise: Frozen sections and stains with sudan III are advisable.

Dr. Wilbert Sachs: In most cases the diagnosis can be made without a frozen section. In necrobiosis lipoidica the process is in the deep part of the cutis and fat, while in granuloma annulare it is usually in the middle and upper parts of the cutis. In necrobiosis lipoidica, although there are giant cells, there are no tubercles, and granular degeneration and necrosis often are not present.

Dr. David Bloom: The color of this patient's lesions did not suggest necrobiosis lipoidica to me. Except for the cutaneous lesions nothing abnormal was detected by thorough examination in the pediatric clinic.

Lichen Planus Confined to the Mouth. Presented by DR. GEORGE M. LEWIS.

Mrs. I. K., a woman aged 39, is presented from the New York Hospital. She had blisters on her lower lip seven years ago. These ruptured and later bled. The mucous membrane inside the cheeks became involved; at times there were soreness and irritation. Soreness and elevation of the lesions of the mucous membranes are apt to be more pronounced at the time of the menses. Her lip cracks readily when the skin is stretched.

The buccal mucosa of both cheeks shows grayish white, irregular, angular and adherent patches. The remainder of the mucous membranes of the mouth are normal. The lower lip is roughened and scaly with some indistinct discoloration.

The Wassermann reaction was negative. A cultural examination did not reveal any fungi (Monilia). The blood sugar content was 75 mg. per hundred cubic centimeters. The diet has been adequate. Administration of vitamin B complex and riboflavin for one month failed to effect any change.

DISCUSSION

DR. DAVID BLOOM: In regard to treatment of lichen planus of the mouth, I believe it will be of interest that one of the two sisters with lichen planus of the mucous membranes of the mouth whom I presented before this society (ARCH. DERMAT. & SYPH. **44**:294 [Aug.] 1941) has responded excellently to injections of liver extract. The other sister, who did not receive any treatment, did not show any changes in the eruption.

DR. ISADORE ROSEN: Cases in which the eruption is limited to the mouth are met with occasionally. They frequently fall into the hands of physicians who refer them for roentgen ray therapy or radium treatment under the mistaken diagnosis of leukoplakia. I have seen some very bad after-effects as a result of this.

DR. MAX SCHEER: Occasionally lichen planus of the mouth will get well, but more often it will persist indefinitely, and I do not believe that any therapy has an influence on buccal lichen planus; at least no constitutional therapy has been of any value in my experience. Treatment of buccal lesions with radiation (roentgen ray or radium) is dangerous, and I know of several cases in which death resulted from such therapy. I know of several cases in which a chronic benign lichen planus became prickle cell epithelioma of the mouth as a result of irradiation.

DR. J. FRANK FRASER: Some years ago Dr. Howard Fox read a paper before one of the medical societies in which he described 10 cases of lichen planus confined to the mucous membrane. I did the histologic work for him in all of those cases, and we found that the picture was identical with that found on the glabrous skin. I might suggest that Dr. Lewis do a biopsy in this case.

DR. GEORGE M. LEWIS: When lichen planus is confined to the mucous membranes it is likely to be confused with leukoplakia. Lichen planus may remain for years on the buccal mucosa without spreading to other parts of the body. The histologic study of the lesion will assist in cases in which a definite clinical diagnosis cannot be determined.

Generalized Lentigo. Presented by DR. ISADORE ROSEN.

V. M., a man aged 20, came to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Sept. 24, 1941 with a generalized eruption of seventeen years' duration.

The patient presents a universal eruption of deeply pigmented macules. These are most numerous on the face and the extensor surfaces of the arms, while on the rest of the body they are less numerous and situated less closely together. The palms and soles are also involved. The mucous membranes are free. The lesions vary in size from that of a pinhead to that of a large pea and are round or oval. Most of the macules are dark brown while others are pale brown.

A brother and a sister also have pigmented spots, but only in a small number. All members of the family are of dark complexion except one sister, who is lighter.

The patient received a thorough examination at the Jewish Hospital in Brooklyn, which he attended from 1937 to 1938. All laboratory tests, including roentgen ray examination of the sella turcica, a Wassermann test, a test of the urine for melanin and determination of the basal metabolic rate, gave normal results.

DISCUSSION

DR. GEORGE M. LEWIS: I have never seen a counterpart of this condition. There seem to be two types of lesions, in one of which there is light pigment and in the other the pigment is dark. I wonder if there will be any tendency later toward malignant degeneration.

DR. PAUL E. BECHET: The lesions are not all flat; many of them are slightly elevated, a fact easily ascertained on palpation. They are brown-black and occur on parts of the body protected from actinic exposure, and while I realize that freckles may be found under similar circumstances, they have when so found been classed as superficial nevi.

DR. SAMUEL PECK: I have never encountered a case like this. It is my impression that if enough lesions were examined microscopically one would find all the graduations from a simple hyperpigmentation of the epidermis that is an ephelis right through to a full formed nevus with nevus cells. One might even find in a few instances the picture of Bloch's pigmented epithelioma. The reason I should be guarded in my prognosis as far as eventual malignant change is concerned is based on the probability that with such an extensive pigment involvement there is a possibility that a few of the lesions are closely akin to melanoma.

DR. WILBERT SACHS: Would one expect malignancy to develop in lentigo occurring so early in life or rather in senile lentigo?

DR. HERMAN SHARLIT: When I first saw this patient I looked for the condition in Jadassohn's "Handbuch der Haut- und Geschlechtskrankheiten." There the name given it is lentiginosa profusa. It is apparently a harmless eruption, and nothing untoward ever happens.

DR. DAVID BLOOM: Freckles and lentigines are frequently confused. A lentigo is a type of flat pigmented nevus.

DR. JACK WOLF (by invitation): My understanding of lentigo is similar to that of Dr. Bloom's, that is, lentigines are nevi and ephelides are freckles. A lentigo may contain nevus cells, but clinically one cannot predict whether nevus cells are present. The term lentigo is purely a clinical one.

DR. DAVID BLOOM: A lentigo may be deeper situated than a freckle, particularly one which is somewhat raised. Treatment of such a lesion will always result in a scar, while that of a freckle will not.

DR. SAMUEL PECK: An ephelis is simply a freckle. In many cases that particular area is the area of normal pigmentation, at least in patients with fair skins and red hair.

DR. WILBERT SACHS: I believe that in a nevus of this type nevus cells would be present but that in lentigo such cells would not be found.

DR. DAVID BALLIN (by inyitation): I should hesitate to traumatize any of those lesions.

DR. ISADORE ROSEN: I never encountered a case like this before. In this particular instance the only way one could come to a conclusion would be to study histologically one, two or three of the different types of lesions. As far as malignancy is concerned, I too feel that it is well not to attempt treatment, as one never knows what will happen. The patient should, however, be observed for a number of years.

Pemphigus Foliaceus. Presented by DR. GEORGE M. LEWIS.

V. M., an Italian aged 36, was first seen at the New York Hospital in August 1941. He stated that one year previously an eruption had appeared on his chest gradually spreading over his body. He noticed blisters forming, but they often

ruptured so quickly that only the remnants were seen. He had mild pruritus. During the past three months there were noticeable loss of weight and some weakness.

The patient presents a generalized eruption consisting mainly of adherent, scaly areas surrounding central zones of redness. Many contiguous areas have coalesced, producing gyrate and configurate lesions. At times a few flaccid bullae can be noted. No lesions are present on the mucous membranes.

The Nikolsky sign was readily obtained. The blood cell count showed 4,900,000 erythrocytes and 9,000 leukocytes; the differential count was as follows: 69 per cent polymorphonuclear leukocytes, 26 per cent lymphocytes, 3 per cent monocytes, 1 per cent eosinophils and 1 per cent basophils. The histologic picture was compatible with the diagnosis of pemphigus. The Wassermann reaction was negative.

Therapy has consisted of injections of sodium arsenate in increasing doses and local application of 2 per cent ammoniated mercury ointment.

DISCUSSION

DR. MAX SCHEER: I agree with the diagnosis of pemphigus but not of pemphigus foliaceus. To me the lesions are those of pemphigus vulgaris.

DR. E. WILLIAM ABRAMOWITZ: My understanding of the foliaceus type of pemphigus is that it is almost impossible to find a bullous lesion. Here the lesions are fairly well circumscribed. Now a few definite bullae may be seen, and I think the condition is pemphigus vulgaris rather than a foliaceus type of pemphigus.

DR. MAURICE J. COSTELLO: I agree with the diagnosis presented, and I think it can be based on the fact that even though the patient has had the disease for six months, his general nutrition is good and there are no lesions of the mucous membranes. I have recently observed several patients suffering from this disease, and this patient presents a feature common to all of them, i. e., semicircinate crusts bordering flaccid bullae.

DR. PAUL E. BECHET: Before being positive of the diagnosis of pemphigus, one should eliminate the consideration of a bullous erythema multiforme; the annular formation and the comparatively short duration favor the latter diagnosis.

DR. HERMAN SHARLIT: I agree with the diagnosis as presented.

DR. FRED WISE: I agree with the diagnosis as presented. Pemphigus foliaceus is associated with bullous and even vegetating lesions in the course of long-lasting eruptions.

DR. GEORGE M. LEWIS: The duration of the disease is one and a half years. The picture changes from time to time. For long periods no bullae can be demonstrated. The Nikolsky sign may be elicited by gentle traction on the skin. I have never seen the Nikolsky sign obtained so readily. For the reasons cited by Drs. Costello and Wise and because the duration of the disease is longer in this case than is usual for pemphigus vulgaris, I believe this case is an instance of pemphigus foliaceus.

Folliculitis Capitis Marginalis. Presented by DR. MAURICE J. COSTELLO.

A. M., a man aged 43, has had an eruption on his scalp along the posterior portion of the hair line for six years.

The eruption is unusual or perhaps unique because of its peculiar linear marginal distribution along the hair line. It consists of a scaly, follicular, erythematous reaction around the hair follicles. A few pinhead-sized keloids are present. There is no clinical atrophy or scarring of previously affected areas. It is cordlike in appearance and measures about 2 mm. in width.

DISCUSSION

DR. E. WILLIAM ABRAMOWITZ: I think the condition in this case should be called folliculitis keloidalis.

DR. MAX SCHEER: I think the name that Dr. Abramowitz suggested is a good one.

DR. DAVID BLOOM: This eruption differs from the usual dermatitis papillaris capillitii. It looks to me like folliculitis sycosiformis, except that instead of pustules there are indurated papulopustules seen in dermatitis papillaris capilitii. Folliculitis sycosiformis of the scalp produces a picture of alopecia which this condition resembles, although no atrophy is seen in the bald area in this case.

DR. GEORGE M. LEWIS: I should like to ask Dr. Costello to explain the nature of the alopecia.

DR. PAUL E. BECHET: While I admit that the linear distribution and the apparent alopecia are both atypical for folliculitis keloidalis, nevertheless I prefer that diagnosis. There are small light to dusky red papules, a few of which have the characteristic induration, and there is some scarring. I have seen folliculitis keloidalis especially in its early stage arranged in linear formation. It is not necessary to observe keloidal formation to make the diagnosis. Keloids appear only in the late stages of the disease, and in mild early stages of the disease they are seldom found. Only a superficial type of scarring similar to that in this case is present.

DR. SAMUEL PECK: The loss of hair in any folliculitis depends on whether or not the inflammatory process involves the hair papilla, so that it is destroyed. If this inflammatory process occurs in a patient with a tendency to keloid formation, there may result a keloidal scar at the site of the hair follicle. It is for this reason that folliculitis keloidalis is so often seen in Negroes.

DR. HERMAN SHARLIT: Is it true that this man had folliculitis in the areas that are now free of hair? In other words, is the baldness due to the disease or is it congenital?

DR. WILBERT SACHS: I cannot make a diagnosis, but I believe that this condition does not fit in with any of the diagnoses suggested thus far. There is neither atrophy nor scarring.

DR. FRED WISE: I do not believe that this condition is an example of ordinary keloid acne. There is an area completely devoid of hair and of visible hair follicles, without evidence of atrophy. It is an unusual form of folliculitis marginalis.

DR. MAURICE J. COSTELLO: The posterior portion of the hair line is abnormal in outline. Its sharp straight margin suggests roentgen ray epilation. The interesting feature is that the area previously involved shows no clinical signs of atrophy or scarring. The eruption has been of similar appearance for six years.

Porokeratosis Mibelli. Presented by DR. ISADORE ROSEN.

J. M., an Italian aged 48, from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, a gardener, is the father of F. M., who was presented with the same diagnosis at the October meeting of this society.

The eruption which the patient presents is located on the fingers and the face and has been present since infancy, according to the statement of the patient. It has never interfered with his occupation and has not inconvenienced him in any other way.

There are fine nickel-sized to quarter-sized lesions located on the thumb, index and middle fingers of the right hand and on the thumb and index fingers of the left hand. The lesions are irregular in shape with gyrate-like configuration. Some parts are considerably hyperkeratotic and partly smooth and depressed, surrounded by a blackish discolored canal-like groove. On the face there are several pea-sized lesions which are telangiectatic and depressed. The patient states that one other lesion situated on one of the fingers has disappeared spontaneously.

Besides the one son who was presented at the last meeting with lesions on the neck and face, there is another son, who has a pea-sized lesion on the right arm suggestive of the same condition.

DISCUSSION

DR. DAVID BLOOM: One boy shows a linear arrangement of lesions resembling a linear nevus in addition to the round and oval lesions seen in the other members of the family. Dr. Satenstein told me that he did not study the pathologic slides thoroughly enough, but from a superficial examination he did not find any relation to the sweat ducts. Absence of relation to the sweat duct does not speak against the diagnosis of porokeratosis, for numerous authors have come to the conclusion that this is not as essential a feature as Mibelli thought it to be.

DR. E. WILLIAM ABRAMOWITZ: Dr. Bloom went to considerable trouble and was rewarded by finding similar lesions in the father and another son. I think this case is a classic one of porokeratosis Mibelli.

DR. FRED WISE: A recent publication by Miescher, of Zurich, points out that the chief change in the epidermis is parakeratosis and that the sweat glands and ducts are unaffected in this condition.

BROOKLYN DERMATOLOGICAL SOCIETY

L. M. WATERHOUSE, M.D., *President*

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Nov. 17, 1941

Sarcoidosis. Presented by DR. ABRAHAM WALZER.

G. W., a Negress aged 22, was presented before the Section on Dermatology and Syphilis of the New York Academy of Medicine in May 1941 (ARCH. DERMAT. & SYPH. **44**:1128 [Dec.] 1941).

DISCUSSION

DR. ABRAHAM WALZER: Since the patient's previous presentation the disease has progressed rapidly, with the possibility of complete involvement of the right eye.

DR. JACOB SKEER: This brings up an interesting observation, namely, that this stage of the disease is a relapse. In general, in sarcoidosis relapses are common.

DR. ABRAHAM WALZER: It is characteristic in sarcoidosis, as in tuberculosis, to have periods of relapses and remissions. This patient now has a relapse, and I think the disease is progressing rather rapidly. There is a notable increase in the number of lesions.

A Case for Diagnosis (Epithelioma?). Presented by DR. JACOB SKEER.

E. G., a Negress aged 25, came to the Cumberland Hospital in August 1941, complaining of a large orange-sized oozing tumor on the right leg of one year's duration.

Several weeks prior to the appearance of this lesion, while the patient was in the South, she became sick with a high temperature and sore throat, for which she received some salty medicine.

Examination showed a tumor 6 by 5 cm. situated on the upper third of the right leg, over the tibia. The tumor was on a broad base, with overhanging edges. The center showed a mushy, warty, granulating ulceration, oozing pus. The lesion bled easily at the slightest trauma, emitting a foul odor. The surface was studded with black pigmentation. Veins were seen radiating from the tumor, which were pigmented, taut and infiltrated.

The Wassermann reaction of the blood was doubtful, and the Kline reaction was 1 plus. The roentgenogram showed no syphilitic manifestations. Microscopic examination showed a loose connective tissue core, lined on both sides by atrophied

squamous epithelium. One surface was relatively normal, except for thickening of the rete pegs and inflammatory infiltrate of the dermis. The other surface showed dyskeratosis and hypertrophy of the rete pegs. There was downward extension of clusters of prickle cells showing pearl formations. The cultures of material taken from the lesion were reported to be growing nonhemolytic streptococci.

DISCUSSION

DR. ABRAHAM WALZER: I think there are three conditions to be considered: bromoderma, mycosis fungoides d'embleé and epithelioma. My impression is that this condition is an epithelioma, but there is a possibility of its being only a bromide eruption. I think that the histologic examination will reveal the diagnosis.

DR. E. A. GAUVAIN: I agree with Dr. Walzer. Without a histologic report, I should make a clinical diagnosis of a bromide eruption, particularly since the patient has had some salty medicine. It would seem that the diagnosis of prickle cell epithelioma is not definite, although, when one considers the duration of this lesion and the fact that it has undergone some transformation, that diagnosis should be taken into consideration.

DR. C. T. CHIARAMONTE: I should not decide on the diagnosis of epithelioma so easily. It would be difficult to distinguish a true epithelioma from hyperplasia. I believe the patient has a superficial or deep fungous infection, and I suggest further studies along these lines.

DR. L. J. FRANK: I agree with the previous speaker. Possibly this condition is a drug eruption, as there is a history of the patient's having taken drugs. A deep fungous infection also cannot be ruled out without further studies.

DR. H. L. FEIGENBAUM: I do not see how one can rule out epithelioma in this case, since there is definite pearl formation. If one thing is definite about a prickle cell epithelioma, it is precisely this feature, and I believe that every histologist is acquainted with this. However, there is nothing to prevent her having a bromide eruption on top of a prickle cell epithelioma.

DR. S. H. SILVERS: I think Dr. Feigenbaum is correct. Malignancy is not the question here. The question remains as to whether there was something else before this malignant growth developed. Whether it was blastomycosis or bromoderma which eventually became malignant is still questionable, but I do not believe one can get away from the fact that the lesion is now a malignant growth.

DR. A. W. GRACE: This extensive ulcer looks definitely malignant to me. It is most important that the histologic status of the lesion be determined as soon as possible. Specimens for biopsy should be taken from the central area of the ulcer, as well as from the cutaneous nodules just lateral to the main lesion.

DR. I. N. HOLTZMAN (by invitation): I suggest another possibility. There are several clinical features about this lesion which are suggestive: first, as Dr. Grace mentioned, the little subepidermal nodules; second, the radiating pigmented striae, and, third, the age of the patient, which is somewhat against a prickle cell epithelioma. I should like to suggest the possibility of a malignant melanoma, which would develop as this lesion has. As far as the pearl formation is concerned, the pearls in the lesion are the most nonmalignant part of it; they are the dead cells.

DR. L. M. WATERHOUSE: I disagree with the diagnosis of melanoma. The condition in this case is of seven months' duration.

DR. JACOB SKEER: All the points brought out in this discussion have been considered. It is possible that Dr. Holtzman is correct in considering the histologic picture as that of a pseudoepitheliomatous hyperplasia.

Acnitis. Presented by DR. LESSER M. FRUCHTBAUM.

A. W., a man aged 50, came to the Unity Hospital with a history of an eruption on his face and scalp of ten years' duration. He stated that the lesions first appeared on the anterior part of the scalp and then spread to the face and chin.

The lesions started as pustules and after healing left depressions. Simultaneously with the appearance of the lesions on the scalp, the hair began to fall. The patient complained of severe itching, which subsided with the application of salves.

The patient shows many pitted, scarred lesions over the entire scalp and face. In addition to alopecia of the scalp there is telangiectasia of the nose, cheeks and ear lobes. The blood vessels of the conjunctiva and sclera are dilated.

The Wassermann reaction of the blood was negative. Reactions to tuberculin tests with dilutions of 1:100,000 and 1:1,000,000 were negative and with 1:10,000 slightly positive.

DISCUSSION

DR. L. M. FRUCHTBAUM: The histologic study did not show anything characteristic of a tuberculous lesion, except for some infiltration of the blood vessels. A mild mercury salve aggravated the condition, but a neutral ointment with 1 per cent phenol helped and the itching subsided. In spite of the fact that there are no acute lesions at present, the process apparently is continuing without remissions. Acnitis seems the most likely diagnosis, because of the pitted scars, the size of the lesions and the progress of the disease.

DR. H. L. FEIGENBAUM: I think this condition is acne varioliformis. The patient has a number of pustules and pitted scars. The location and the history of a continuous process would, it seems to me, confirm this diagnosis.

DR. E. A. GAUVAIN: I also believe this case is one of acne varioliformis. The follicular lesions are acutely inflammatory. The scars on the scalp are thicker than one usually finds in the tuberculids, and they are varioliform.

DR. J. SCHWEIG: I agree that the condition is acne varioliformis, with a definite picture of the characteristic symptoms. It is a superficial papulopustular eruption confined to the follicles, which undergo central necrosis and terminate in fairly large, pitted scars. It is limited to the scalp, temples and forehead, with new groups coming in periodically. It usually lasts many years. According to the textbooks, it should heal with local applications of ammoniated mercury, but this is not always true, as in many cases the disease is intractable. It is self limited and after a period of years becomes quiescent.

DR. A. W. GRACE: I think this disease is acne varioliformis. Histologic examination does not show any tuberculous structure.

DR. M. M. ESTRIN: Neurotic excoriations should also be considered. Many patients continually dig with their nails because of itching until various forms of pustules develop, which later form deep scars. However, I believe this case is one of acne varioliformis.

DR. A. J. EPHRAIM (by invitation): I think the condition in this case is acne varioliformis. I believe that it is necessary to continue treatment after the lesions have disappeared in order to avoid a recurrence.

Dermatitis Medicamentosa (Bismuth?). Presented by DR. A. WALZER.

J. M., a 64 year old cabinet maker, presented for Dr. A. Blau, was admitted to the Department of Health Clinic with a diagnosis of late latent syphilis. Injections of bismuth subsalicylate were started April 16, 1941. The patient received fourteen injections from that date to October 15, when the eruption was first noted. The patient states that moderate itching first manifested itself in June, when the eruption began. The eruption is located in the sacral area and on the back and sides of the chest, all extremities and the penis. There is a large lesion in the left supraclavicular region. The eruption consists of sharply demarcated patches of different shapes, varying in size from that of a pea to that of a dime. Some are macular; others are infiltrated and red. Some have raised borders. Some have coalesced to form bizarre figures. The histologic diagnosis was "chronic dermatitis, toxic in origin."

Since the cessation of treatment the lesions have improved. There is no history of any other drug having been taken by the patient.

DISCUSSION

DR. A. BLAU (by invitation): Today the lesions are much improved. Many have entirely disappeared; others are not as infiltrated as formerly. The pruritus, which was never great, is not present now.. The histologic picture is consistent with that of a toxic drug eruption.

DR. JOEL SCHWEIG: My impression is that this case is one of toxicoderma. It is of course important to make a thorough investigation of all drugs taken in the form of medicine or food. The clinical manifestations are more suggestive of drugs belonging to the phenolphthalein, antipyrine or phenobarbital groups. Last year I presented a similar case (Dermatitis Medicamentosa [Phenolphthalein], ARCH. DERMAT. & SYPH. **44**:973 [Nov.] 1941), in which there were annular, infiltrated patches, presenting distinctive features of a premycotic eczema. However, the infiltrations turned out to be edema, which later subsided, leaving pigmentation. Another histologic study should be made in this case to rule out a premycotic eczema.

DR. A. W. GRACE: I have seen bismuth toxicoderma in a patient under treatment for syphilis, who had had a mild dermatitis during the preceding course of neoarsphenamine. The eruption due to bismuth took the form of large urticarial wheals, situated chiefly on the back. Therapy was discontinued altogether for a few months, and the urticarial manifestations disappeared. The wheals recurred on resumption of bismuth therapy. Persons who are intolerant of the arsphenamine drugs are liable to exhibit intolerance of bismuth.

DR. M. M. ESTRIN: I wrote to Merck's asking for a complete analysis of the bismuth compound they sold, and they gave me a list of fifty to sixty impurities present in their preparations. Any bismuth that one buys contains impurities, and an eruption may be caused by any one of these impurities.

DR. C. T. CHIARAMONTE: I believe there is such an entity as a bismuth dermatitis. In all the cases that I have observed there have been lesions on the forearms and arms, especially on the extensor surfaces, resembling erythema multiforme; others were distinctly eczematous and vesicular. In all there were some lesions which were definitely demarcated. In 1 woman under my care two years ago such an eczematous eruption developed on the forearm with each of two successive courses of bismuth therapy. I am well aware of the fact that arsenic may be among the impurities in bismuth, but I do not believe the eruptions are due to arsenic.

DR. E. A. GAUVAIN: I am convinced that there is such a thing as a bismuth dermatitis, although it is rare. I feel that the condition in this particular case is a drug eruption, probably due to bismuth, and not mycosis fungoides, as casual examination would suggest.

DR. A. WALZER: When the patient was first seen at the clinic, mycosis fungoides was suggested. But the story of the eruption's association with the administration of bismuth is definite. There is no particular reason to incriminate arsenic in this case. I do not think any one has seen an arsenical eruption of this kind.

DR. D. M. DAVIDSON: I saw this patient twice at the clinic. The first time I believed the diagnosis to be either a drug eruption or possibly mycosis fungoides. Seven days later, when I saw him again, almost 25 per cent of the lesions had gone, leaving pigmentation, while the other lesions were somewhat edematous. In view of the fact that lesions of mycosis fungoides do not disappear so quickly and are more infiltrated, I was influenced toward making a diagnosis of drug eruption. From the history of the case it would seem that the drug in question is bismuth. The only way of proving it is to stop giving the injections of the bismuth compound and after the disappearance of the lesions to start giving the injections again.

DR. A. BLAU (by invitation): Bismuth eruptions must be rare, because in a large syphilis clinic the question arises frequently. Arsenic as a contaminant of bismuth can often be ruled out, as the patient does not show intolerance to the arsphenamines. In this case if, after clearing up, the eruption recurs with the use of bismuth, I think one must assume that it is due to bismuth.

Poikiloderma Atrophicans Vasculare (Jacobi). Parapsoriasis? Presented by DR. A. WALZER.

S. B., a woman aged 40, presented for Dr. I. N. Holtzman, complained of a generalized itching eruption of twelve years' duration. The eruption began on the right thigh and was accompanied by itching, which was particularly severe in cold weather. Other patches have appeared progressively since then until now the entire trunk, left side of the face and bridge of the nose are involved.

On the aforementioned areas there are red, well defined, noninfiltrated patches, consisting of a conglomeration of erythema, slight scaling atrophy with wrinkling of the skin and fine telangiectases.

DISCUSSION

DR. H. L. FEIGENBAUM: I agree with the diagnosis as presented.

DR. D. M. DAVIDSON: The lesions on the breast show the features of poikiloderma of Jacobi. The lesions on the thighs, however, which are of ten years' duration, consist of large erythematous patches with a faint scaliness and possibly an atrophic epidermis in places. My impression of the lesions on the thighs is that of parapsoriasis. I believe that the condition is not poikiloderma of Jacobi but rather, possibly, parapsoriasis with poikiloderma-like changes.

DR. L. M. FRUCHTBAUM: Poikiloderma atrophicans vasculare (Jacobi) is not a disease entity but a symptom complex. In addition to the maculopapulosquamous lesions on the trunk, there is scaling of the scalp, with little itching. The history of so many years' duration in this case is in favor of parapsoriasis, which I believe will be confirmed by histologic studies.

DR. I. N. HOLTZMAN (by invitation): I am willing to accept the diagnosis of parapsoriasis.

A Case for Diagnosis. Presented by DR. LAWRENCE M. WATERHOUSE.

G. F., a man aged 36, presented himself seven months ago complaining of a small pimple on the left buttock, which after being scratched, gave him a great deal of trouble for the next three months around the rectum and on the perineum. He was treated by a physician for two months before he consulted me, about a month and a half ago.

On the perineum, extending from an area about the anus to the inguinal regions anteriorly, there are masses of thickened and edematous skin and numerous suppurating sinuses and fistulas.

The patient received ultraviolet irradiation, sulfanilamide and four treatments with roentgen rays (total, 300 r).

The reactions to the Frei test, the Wassermann test of the blood and the tuberculin test, with a dilution of 1:1,000, were all negative.

DISCUSSION

DR. A. WALZER: It is difficult to make a diagnosis at this time. The lesion makes me think of sporotrichosis. That was my first impression. However, I have never heard of or seen such lesions in this location. I suspect a fungous infection of some type, probably sporotrichosis.

DR. A. W. GRACE: I think this man has nothing more than a pyogenic infection of the subcutaneous tissue, burrowing and producing sinuses. It is likely that he also has fistula in ano. I have had 2 women under observation for the

past year with lesions similar to those presented, which began as small pustules in the perianal and perivaginal areas. Excision of the sinuses or of the entire involved area is the most satisfactory form of treatment.

DR. C. T. CHIARAMONTE: I believe the patient has hydradenitis suppurativa. The suppurating sinuses are typical, and apocrine glands are normally located in the area involved.

DR. A. WALZER: I suggest giving large doses of potassium iodide as a therapeutic measure.

DR. L. FRUCHTBAUM: The lesions seen in this case are sinuses probably originating in the rectum. A definite diagnosis can be made by injecting the sinus with an opaque liquid and taking roentgenograms. The treatment is excision of the sinus tracts.

DR. D. M. DAVIDSON: The clinical appearance of the lesions, especially the scarring, suggests that the condition is lymphogranuloma venereum. Although a Frei test was performed and the reaction was negative, I suggest a repetition of the test. I should also like to call attention to the fact that in a small percentage of cases of lymphogranuloma venereum there is a negative reaction to the Frei test, which is said to be due to an anergic state.

DR. L. M. WATERHOUSE: When I first saw this patient I strongly suspected lymphogranuloma. The condition seems to me to be pyogenic infection, stemming possibly from an anal fistula.

A Case for Diagnosis (Pemphigus?). Presented by DR. L. J. FRANK.

W. S., a 45 year old barber, complained of soreness of the throat and mouth of four months' duration.

Examination shows superficial ruptured bullae on the pharynx with a raw red base and edema of the entire area. The teeth are in poor hygienic condition; the tongue is coated.

A smear for Vincent's organisms was negative. The urine was normal; the Wassermann reaction of the blood was negative. A complete blood count was within normal limits.

DISCUSSION

DR. E. A. GAUVAIN: I do not believe there is sufficient proliferation of the tissues or foul odor of the mouth to warrant the diagnosis of pemphigus.

DR. A. WALZER: The lesions of the mouth are peculiar. There are erythematous areas surmounted by distinct vesicles. The right side of the mouth, if seen alone, would strongly suggest pemphigus. I should hesitate to label a condition pemphigus unless I was sure of the diagnosis. Drug eruptions should first be excluded.

DR. H. H. SAWICKY (by invitation): Although pemphigus is a possibility, I think there are many features which suggest a different diagnosis. The man has a definite inflammatory condition. The vesicles on the roof have an erythematous base. He has inflammation of the tonsils with a lot of white patches, and in addition his gums bleed easily. I think he should be given thorough therapeutic tests for Vincent's infection.

Acanthosis Nigricans. Presented by DR. A. WALZER.

C. D., a man aged 50, presented for Dr. I. N. Holtzman, complained of itching of the perineum of three years' duration.

The skin of the perineal raphe and of the medial parts of the apposing surfaces of both thighs shows hyperpigmentation and symmetric elevation of the cutaneous folds, maximal in the center of each area, into papillomatous-like lesions. The lesions are velvety and without any lichenification or ulcerations. In the right axilla is a pedunculated fibroma, with hyperpigmentation of both axillas and cubital fossae.

The liver is palpable 2½ fingerbreadths below the costopleural margin. There is no tenderness or associated gastrointestinal complaints.

A histologic section of skin from the left thigh showed hyperkeratosis of the overlying stratum corneum. The basal layer showed some hyperpigmentation, and there were numerous pigment-laden chromatophores in the cutis.

DISCUSSION

DR. A. WALZER: Tonight the patient shows symmetrically arranged areas on the medial aspects of the thighs. The microscopic study showed acanthosis with pigmentation. He was investigated thoroughly. The only other abnormality was a large liver, about 2 fingerbreadths below the costophrenal margin. This case may be an ordinary one of acanthosis. In adults, in about 25 per cent of the cases there is no associated malignant growth.

DR. J. SCHWEIG: I believe that this condition is acanthosis nigricans of the adult type. The lesions are symmetrically arranged, and the patches are dark brown and covered with a papillomatous growth of velvety appearance. Of course microscopic study will establish the diagnosis, since the cutaneous histologic picture is characteristic. The prognosis in cases of this kind is uncertain and should be guarded, as malignant growths not present at the time when the cutaneous manifestations appear may occur later. This point was emphasized by O'Leary (In discussion on Herold, W. C.; Kaufman, W. H., and Smith, D. C.: Acanthosis Nigricans, ARCH. DERMAT. & SYPH. **44**:798 [Nov.] 1941). In 3 of his cases of acanthosis nigricans laparotomies were performed in order to recognize and treat early malignant growths of the internal organs. The operations showed no evidence of cancer at the time; however, in 1 after five months and in another after a year carcinoma of the stomach developed. The third patient is still alive and, so far, well. I feel that this case should be studied thoroughly and watched closely for early manifestations of carcinoma.

DR. E. A. GAUVAIN: I believe that a patient with acanthosis nigricans of three years' duration and associated malignant growths would not be in such a healthy condition. I think the lesions in this case are traumatic.

DR. A. WALZER: What is the relation between acanthosis nigricans and Addison's disease? Between pigmentation and verrucous lesions? Some believe that verrucous lesions always occur on pigmented areas; others say that verrucous lesions can occur independently of pigment.

DR. A. W. GRACE: I had occasion to make a careful study of a case of acanthosis nigricans about seven to eight years ago. The picture was different from that shown by this patient, who, I think, does not have this disease. My patient died from carcinoma of the liver, which may have been primary in that organ. At autopsy no histologic change was found in any endocrine gland. Extracts of the adrenals, pancreas and pituitary were injected into various animals, without producing any pigmentary change in them. The patient presented has multiple soft fibromas in the perineal region and groin which could readily be removed by electrodesiccation.

DR. L. FRUCHTBAUM: The lesions in acanthosis nigricans are scattered over the entire body, distributed symmetrically and pigmented. However, the lesions in this case resemble those of verruca acuminata.

DR. I. N. HOLTZMAN (by invitation): The resemblance to lichenified dermatitis is only superficial. The lesions are sharply demarcated, and feel like those described in acanthosis nigricans. The only perplexing feature is the sharp localization. One other case of acanthosis nigricans is now under observation at the Brooklyn Cancer Institute; there is typical pigmentation in the groins and axillas. Interestingly enough, in the past few months verrucae have developed on the entire body, which leads me to suspect that the verrucous element is not connected with the hyperpigmentation.

CHICAGO DERMATOLOGICAL SOCIETY

LEONARD F. WEBER, M.D., *President*

MICHAEL H. EBERT, M.D., *Secretary*

Nov. 19, 1941

Acrodermatitis Atrophicans. Presented by DR. ARTHUR W. STILLIANS.

A nurse aged 64, of Swedish birth, had pains in the sternum and shoulders in 1906 which resulted in the formation of a large mass on the right side of the sternum at the height of the third costal cartilage. Some years ago she noticed red swellings on the ankles which slowly progressed up the legs and thighs. These swellings were painless and not tender. Later the same process attacked the backs of the hands and spread upward above the elbows. Within the last twenty years she has had three epitheliomas on the face which were cleared up by curettage, cautery and irradiation.

Examination of the blood showed hemoglobin (Sahli) 92 per cent, erythrocytes 5,430,000 and leukocytes 6,000, with a differential distribution of 1 per cent band neutrophils, 60 per cent segmented neutrophils, 36 per cent lymphocytes and 3 per cent monocytes. The sedimentation rate was 20 mm. in an hour. The Kahn reaction was negative. The calcium content of the blood was 8.85 mg. per hundred cubic centimeters. Roentgenograms of the long bones showed no deficiencies but a slight osteoarthritis of the knees and of the joints of the fingers. Roentgenograms of the chest showed a mass of egg size, like an interstitial fibroma with a small amount of bone in it, apparently derived from the anterior wall of the gladiolus.

Beginning at the distal third of the dorsum of the left foot the skin is thin, dark red, loose and wrinkled. About the left ankle and along the left shin it is glossy and tight and the underlying tissue is hard but not swollen and not pitting on pressure. About the ankle, especially on its outer side, and on the distal third of the shin the skin is gray. Above this, over the shin, it is yellowish with many brown spots. Small varicosities show distinctly, and there are several hemispherical varices about 1 cm. in diameter. These varicosities have been treated and much benefited by injections of saline and dextrose solution. On the knee the skin is thin, loose, wrinkled and bluish red. On the thigh are many round, dull red, slightly indurated patches up to 4 cm. in diameter, giving a blotchy appearance. These extend nearly to the groin. From one of these a specimen was removed for microscopic study. The right leg is similarly affected but to a lesser degree. On the backs of the hands and extending up the ulnar side of the forearms and part way up the outer side of the arms is a similar change in the skin. On the back of the left hand is one of the hemispherical varices. The skin on the elbows is especially atrophic and darker than that about it, and there is a large oval induration distal to each elbow.

Histologic examination of the specimen removed showed little change in the epidermis except looseness of the stratum corneum. There was edema of the upper part of the corium, and below the papillary layer were foci of infiltrate made up of lymphocytes and connective tissue cells, with an occasional plasma cell. The lymph spaces were dilated. Thick bands of the same sort of infiltrate accompanied the sweat ducts, hair follicles and blood vessels into the deeper portion of the corium. The blood vessels were thickened, and some of them were obliterated. The elastic tissue was nearly absent from the papillary layer and was badly shattered in the deeper part of the corium.

DISCUSSION

DR. M. J. REUTER, Milwaukee: I agree with the diagnosis of acrodermatitis chronica atrophicans. I wonder if one is correct in labeling this disease as such. The original description by Herzheimer included various ill defined nodules and

infiltrations. I believe diffuse idiopathic atrophy would be the more correct term to use in this particular case.

DR. MAURICE OPPENHEIMER (by invitation): This case is a typical instance of this condition. I do not agree that the name idiopathic atrophy should be used, because the first phase is inflammation. This condition should be called dermatitis atrophicans idiopathica diffusa progressiva. This case shows atrophic macules on both sides, acrofibromatosis, infiltrative changes on the arms and pseudoscleroderma tic changes on the legs. The histologic slide reveals the typical stage of infiltration. The elastic fibers are completely absent, which is characteristic for this disease.

Necrobiosis Lipoidica Diabeticorum. Presented by DR. MAURICE DORNE and DR. S. J. ZAKON (by invitation).

F. G., a Jewess aged 43, presents a single lesion on the dorsum of the right foot. The lesion, a plaque, is polycyclic in outline and sharply defined and measures 4 by 5 cm. It feels firm, much like a patch of scleroderma. The surface is shiny and covered with adherent scales. The border is violaceous and the center shows areas of necrosis. She first noticed the lesion about ten months ago as a pinhead-sized papule.

The patient presented no other symptoms of diabetes. There is no history of diabetes in the family.

Urinalysis showed 8.3 mg. of sugar per hundred cubic centimeters. The sugar content of the blood was 217 mg. per hundred cubic centimeters, and the cholesterol content was 179 mg. The Wassermann reaction of the blood was negative.

Histologic examination showed the changes of necrobiosis lipoidica diabeticorum.

DISCUSSION

DR. MARCUS R. CARO: I agree with the diagnosis both clinically and histologically.

DR. S. J. ZAKON (by invitation): The reason for presenting this case was that this patient had not known she had diabetes. This was the first time she was examined, and a diagnosis of necrobiosis lipoidica diabeticorum was made before laboratory examination disclosed her diabetes.

Urticaria Papulosa Perstans. Presented by DR. MAURICE OPPENHEIM (by invitation) and DR. D. COHEN (by invitation).

Mrs. M. T., a white woman aged 33, a housewife, presents a generalized intensely pruritic eruption of about two years' duration. The extensor surfaces of the extremities are more involved than the trunk and face. Papules up to the size of a pea are present, sharply limited, round and light red. Some lesions have crusts. No dermographia is present. The lesions disappear under pressure with glass.

Two years ago the patient had a blood transfusion, which was followed by pruritus about the cubital space and later about the ankles. Shortly thereafter lesions began to appear below the knees and elbows, and after three or four months dissemination took place. Treatment in the past has consisted of application of various ointments, administration of solution of potassium arsenite U. S. P., injections of bismuth compound and histamine and a short course of roentgen therapy on one arm and leg.

Examination of the blood revealed: 5,050,000 erythrocytes; 9,500 leukocytes, with a differential distribution of 55 per cent polymorphonuclear leukocytes, 9 per cent eosinophils, 25 per cent lymphocytes and 11 per cent monocytes; 41.6 mg. of nonprotein nitrogen per hundred cubic centimeters, and 10.0 mg. of calcium. The urine was normal, and no parasites or ova were found on examination of the stool.

Histologic examination revealed hyperkeratosis, thickening of the stratum granulosum and definite acanthosis. There were an elongation of the papillae, dilated capillaries in the papillary layer and lymphocytic infiltration about the dilated vessels in the subpapillary layer and in the cutis. There was also lymphocytic infiltration about the blood vessels and glands. Edema was present in the subpapillary layer and in the cutis. Connective tissue showed little eosinophilia.

At present the treatment consists of ultraviolet irradiation, injections of calcium gluconate, oatmeal baths and a condiment-free diet. Locally a menthol-alcohol lotion is being applied.

DISCUSSION

DR. OLIVER S. ORMSBY: I suppose the title used by the presenters fits the foreign viewpoint of conditions of this kind. The group as a whole which has been described under various titles presents a confusing picture. Some years ago I had the privilege of working on a case in which there were lesions of the type shown on the extremities of this patient. Urticaria perstans verrucosa was considered, but after a histologic examination the case was recorded under the title prurigo nodularis by Dr. Hyde. Cases of this type had been reported by Schamberg under the title multiple tumors of the skin accompanied by intense pruritus. In the present case the intense itching limited to the lesions, their physical characteristics and their persistence are characteristic of prurigo nodularis.

DR. MARCUS R. CARO: I observed this patient for about a year with the diagnosis of prurigo nodularis. I believe that the diagnosis and prognosis are the same as under the title presented. It seems to me that she still has all of her original lesions. I saw her in the beginning when the lesions were small papules. Many of these have since then become thick nodules. As for the presence of facial lesions in this disease, I have another patient with prurigo nodularis under observation who has many characteristic lesions on the face as well as on the body and extremities.

DR. FREDERICK R. SCHMIDT: I think from a clinical and prognostic standpoint one should consider the possibility of aleukemic leukemia, for possibly later there may be some change in the blood. I have seen nodules not as widespread as these in cases of proved leukemia.

DR. MAURICE OPPENHEIM (by invitation): There is much confusion concerning urticaria and prurigo. They should be separated. There are acute and chronic forms of urticaria. The acute forms are classified according to the intensity: urticaria simplex, lichen urticatus and strophulus, mostly observed in babies and little children. The urticaria acuta in adults can be classified as urticaria simplex, urticaria annularis, urticaria figurata, urticaria porcellanea and urticaria gigantea. The latter leads to angioneurotic edema. The chronic forms of urticaria are urticaria recidivans cum pigmentatione and urticaria papulosa perstans. One form of the latter is called urticaria perstans verrucosa, and another form is called acne urticata (Kaposi). The histologic pictures are not very characteristic. There are edema in the papillary and subpapillary layers, enlargement of capillaries and precapillaries and lymphocytes, leukocytes, mast cells and plasma cells in various number. In urticaria perstans there are hyperkeratosis, sometimes elongation and shrinkage of the papillae and sometimes verrucous formations and superficial necrosis.

In prurigo Hebra, which starts in early childhood, in Vienna frequently when children are taken from the nipple and fed artificially, the typical lesions seen are the so-called prurigo nodules. These are round, the size of sago corn, yellow or brown and better felt than seen; there is present a high degree of itching, and therefore they are soon scratched off and covered by bloody crusts. Two forms are distinguished, prurigo mitis and prurigo ferox, depending on the complications with impetigo and eczema. The typical location is on the extensor surfaces of the extremities and on the forehead. In consequence of long scratching, lichenification and glandular induration, particularly of the femoral glands, are encountered.

Lichen chronicus simplex is strictly separated from urticaria and from prurigo. In my opinion, prurigo nodularis of Hyde must be completely separated from

prurigo Hebra according to this description, and I think it would be better not to use this name and to consider the condition as a certain type of urticaria papulosa perstans.

Urticaria pigmentosa does not belong to these groups; it is rather a nevoid disease.

Dermatitis Factitia. Presented by DR. EDWARD A. OLIVER and DR. S. M. BLUEFARB (by invitation).

A. G., a man aged 68, presented himself at the dermatologic clinic of the Northwestern University Medical School on Jan. 1, 1941 with small papules on the right ankle. Treatment consisted of elixir of phenobarbital orally and zinc oxide ointment locally. The dermatitis did not respond to this treatment, and the condition then extended to both lower extremities, with an eczematized dermatitis. He was given sodium thiosulfate, 15 grains (1 Gm.), intravenously three times a week, and a bismuth cream was applied locally. There was no improvement in the dermatitis, and a boot of Unna's paste (hard paste zinc oxide N. F.) was then applied to each leg. The dermatitis then improved; however, when the paste boots were removed the dermatitis reappeared, and it was thought best to have the boots on permanently. On November 14 the patient complained of papules on the right elbow. A fixed dressing was then applied to the forearms. He stated that the following day the bandages became too tight and he noticed that on removal of the bandages his forearms and hands were swollen and large "blisters" were present.

Clinically, he now presents linear and streaked bullae on both forearms. Some of the bullae are filled with a serosanguineous fluid. Paste boots are present on both lower extremities.

DISCUSSION

DR. A. W. STILLANS: I did not see any reason to disagree with the diagnosis, especially in the light of the patient's removing the fixed dressings.

DR. FREDERICK R. SCHMIDT: I saw this patient for two years, and never until today did he show bullous lesions. The condition has always been a simple dermatitis.

DR. EDWARD A. OLIVER: This condition is such a good example of factitious dermatitis that we felt the patient should be shown. Whenever we applied occlusive dressings to the legs, the lesions promptly healed, but they reappeared shortly after removal of the dressings. The bullous eruption on his arms is a typical factitious dermatitis.

A Case for Diagnosis. Presented by DR. EDWARD A. OLIVER and DR. M. A. GOLD (by invitation).

The patient, a Negro aged 48, is an inmate of the Veterans Administration Facility, Hines, Ill., and has hypertensive heart disease in addition to his eruption. The present eruption began approximately six years ago. Previous to its occurrence he had been taking a preparation known as 666 for colds and for its laxative effect (666 contains iron, quinine, caffeine citrate and magnesium sulfate and no phenolphthalein). He is a habitual user of cathartics and takes some preparation, such as ex-lax, Carter's liver pills or salts, every other day. He has taken these preparations for years but states that he did not take any of them previous to the appearance of the eruption.

The lesions cover almost the entire body and consist of macular areas varying in size from that of a dime to that of a quarter and a half-dollar. They are dark bluish black in the center with a reddish blue periphery. The more recent lesions on the arms and on the abdomen suggest erythema multiforme or erythema perstans. The eruption involves the extensor aspects of the arms, the elbows, the trunk and the legs. The large patches which are present on the shins, thighs, buttocks and posterior aspects of the thighs are covered with dry adherent scales.

The Wassermann reaction was negative, and the urine was normal.

DISCUSSION

DR. EDWARD A. OLIVER: We gave the patient fairly large doses of phenolphthalein about a week ago, and there was no exacerbation of the lesions.

DR. HERBERT RATTNER: The clinical picture suggested a drug eruption, probably a fixed eruption. The patient's story is not necessarily reliable. On several occasions when I suspected an eruption to be due to phenolphthalein the administration of that drug alone failed to provoke a flare-up, but a flare-up did result from the ingestion of the whole medicine. Apparently in such cases the eruption is the result of a synergistic action.

DR. S. W. BECKER: I looked at the microscopic section and there was surprisingly little in the section compared with the clinical appearance of these fairly thickened plaques.

DR. EDWARD A. OLIVER: The section was taken from the lesion on the flexor aspect of the right forearm.

DR. S. W. BECKER: The section did not show edema, which one would expect in a fixed drug eruption.

DR. LESTER M. WIEDER, Milwaukee: I recall seeing recently a fixed eruption produced by magnesia magna following magnesia sensitization. These lesions were similar to the ones produced by other drugs. I have noticed reports of such instances in the proceedings of the New York Dermatological Society.

DR. S. W. BECKER: It is possible that this milk of magnesia may be fortified, because phenolphthalein is placed in many of these preparations.

DR. EDWARD A. OLIVER: I, too, believe that this condition is a fixed eruption. The patient's history may be unreliable. I spent considerable time in questioning him about the drugs he had taken before the appearance of the eruption. He stated that he had taken nothing but the preparation known as 666.

Pemphigus Erythematodes (Senear-Usher). Presented by DR. L. M. WIEDER, Milwaukee.

L. R., a Jew aged 41, noted first lesions on the upper part of the back about Aug. 15, 1941. These were shortly followed by lesions on the cheeks, forehead, back and chest, in the axillas and around the umbilicus. Most of the lesions began as flaccid superficial vesicles and small bullae, which dried quickly, forming a firm, wafer-like crust which usually separated as one piece, leaving an erosive base, accompanied by itching and often by pain. Other lesions, especially on the upper medial portions of the cheeks, have appeared as ill defined, dully inflammatory, scaling, small coin-sized patches. No mucosal lesions have been found. The only previous disease of the skin was an attack of follicular impetigo or pustular folliculitis of the bearded region about twenty-five years ago. The patient had also observed before the onset of the present condition that the scalp was often dry and slightly scaly. There have been no systemic symptoms.

The urine, a complete blood count and the sedimentation rate were normal. There has been little or no improvement following roentgen therapy and administration of a solution of potassium arsenite U. S. P.

On histologic examination, the horny and granular layers were missing. The prickle cell layer was edematous throughout, with liquefaction necrosis of the surface cells and sparse migratory leukocytes in the rete layer. There was mild acanthosis; the basal layer was intact. The collagen fibers were edematous in the papillary and subpapillary layers, and there was a sparse polymorphous leukocytic infiltration, chiefly perivascular, throughout the upper part of the corium.

DISCUSSION

DR. FRANCIS E. SENEAR: I thought the condition in this case was an interesting example of the group of diseases considered as pemphigus erythematosus because at the onset it did have an appearance which Dr. Wieder and his associates took to be lupus erythematosus. There are still some remains of the first lesions on the

knees and cheeks. It is possible that the treatment used has caused these to undergo involution. On the other hand, this may be a spontaneous remission, since the facial picture often changes rapidly in pemphigus erythematosus.

The eruption on the body is definitely bullous. Bullae are seen in relatively few cases; a keratotic type of eruption is much more common. One of the bullae resembled those shown in the photograph Dr. Ormsby showed of one of his earlier cases. The Nikolsky sign in this case is more easily demonstrable than in cases of pemphigus vulgaris.

I had under observation at the University a patient with typical pemphigus erythematosus. The condition changed to typical pemphigus vulgaris, and he died within a very few months.

In view of the short duration, the character of the primary lesions—even though there are bullous lesions in some cases in which the condition is chronic—and the Nikolsky sign, typical pemphigus vulgaris might develop in this case. This case in my opinion serves to clinch the fact that there is such a disease as pemphigus erythematosus. Pathologically there is no sign of lupus erythematosus.

Dr. Oliver S. Ormsby: This form of pemphigus is recognized generally except by some Eastern colleagues. Their conception is that this condition is lupus erythematosus with bullous lesions. This entity is easily recognized, but it is also known that the condition is different both clinically and histologically from the pemphigus under discussion.

Dr. Lester M. Wieder, Milwaukee: I presented this case because the condition is an early as well as a fairly typical example of a clinical entity of which only some fifty-odd cases are recorded. Also, considerable controversy has existed over the question of whether this disease is a variant of pemphigus or disseminated lupus erythematosus. This patient's eruption was only one month old when I first saw him, and the involvement of the butterfly area of the face together with the absence of definite bullae on the upper part of the back and chest led me to make a provisional diagnosis of disseminated lupus erythematosus. However, even then there was a positive Nikolsky sign. Subsequently, the eruption evolved into the typical clinical picture of pemphigus erythematosus. The bullae have always been evanescent, and I have not observed a fresh unruptured bulla until today. Post-bullous erosions have been continuously present, and the Nikolsky sign has been increasing in intensity. Concerning the pemphigus versus lupus erythematosus question, the biopsy in this case definitely rules out lupus erythematosus. In their review of this disease, Wile and Holman reported that of 9 patients who died, 5 died with the clinical picture of pemphigus and 2 with that of acute disseminated lupus erythematosus; for the other 2 the details were not stated. Granting that the 2 patients who apparently died of acute disseminated lupus erythematosus may have had the bullous form of that disease, the balance of evidence would appear to place pemphigus erythematosus as a comparatively rare clinical variant of true pemphigus, with confusion arising from the difficulty of assigning to pemphigus itself the lesions of the Senear-Usher syndrome resembling seborrheic dermatitis and discoid lupus erythematosus.

A Case for Diagnosis (Systematized Nevus?). Presented by Dr. David Kahn (by invitation) and Dr. S. W. Becker.

J. G., a 27 year old American of Italian parentage, has had a generalized dermatosis since birth. Brownish yellow grouped papular lesions are present on the entire body with the exception of the face, hands and feet. Extremes of temperature cause the lesions to appear more elevated, darker and somewhat reddish. The lesions appear less distinct when the skin has been tanned.

No consanguinity or prenatal abnormality is present in the family.

The lesions consist of irregular patches of grouped round and irregularly shaped papules and seem to follow the normal lines of cleavage. At times some of them appear brownish red or livid. The axillary lesions are slightly vegetative. There is pitting of the nails.

The urine was normal. The Kolmer and Kahn reactions of the blood serum were negative.

Histologic examination of a section removed from the thorax showed epidermal atrophy with an increased number of blood vessels in the superficial portion of the dermis. About the blood vessels and in the superficial part of the dermis were acidophilic mononucleated cells and fibroblasts. The deeper part of the dermis showed a large island of sweat gland elements in the adipose tissue. A section from an atrophic lesion on the calf revealed slightly thinned epidermis with the same variety of infiltrate, consisting of eosinophilic mononuclear cells and fibroblasts. The blood vessels were slightly increased in number.

DISCUSSION

DR. M. R. CARO: In the histologic section there are sharply circumscribed nests of cells which look like mast cells, although staining with polychrome methylene blue would demonstrate their identity more clearly. This suggests the possible diagnosis of urticaria pigmentosa, although I have never seen urticaria pigmentosa with follicular accentuation as is present in this case. When a lesion was stroked it became urticarial and red, and this, added to the histologic picture, makes the diagnosis of urticaria pigmentosa likely.

DR. MAURICE OPPENHEIM (by invitation): I agree with Dr. Caro in this case. It is necessary only to make a staining for mast cells, because aggregated mast cells (mast cell tumors) are characteristic of this disease. The dermographia and the color struck me as indicating some peculiar form of urticaria pigmentosa. It is known that this disease usually disappears after some time. It is seen in children but seldom in adults. The papules consist of aggregations of pale lichen-planus-like efflorescences.

DR. S. W. BECKER: When I first saw the section, with the stain which we used the mononuclear cells were eosinophilic rather than basophilic. They had the morphologic characteristics of basophilic cells seen in urticaria pigmentosa. The lesions on the thigh are erythematous. Here there was distinct epidermal atrophy. I think the disease is probably some unusual variety of urticaria pigmentosa.

A Case for Diagnosis. Presented by DR. MICHAEL H. EBERT.

A. B., a Negro aged 47, stated that two weeks ago, a group of vesicles developed in the left genitofemoral region. These caused no sensation. Two days later similar lesions appeared in the scalp and on the face. New lesions have continued to appear. Some ammoniated mercury ointment was used on the face, which caused irritation.

In an area 6 inches wide (15 cm.) on the inner surface of the left thigh and involving the genitofemoral fold there is a group of coalesced vesicles. At the border these are discrete, match head sized to split pea sized, umbilicated and filled with cloudy fluid. Some are hemorrhagic. The whole area is edematous and reddened. Discrete umbilicated vesicles are scattered over the face and neck. There is a group of these vesicles in the axilla. There are crusted relics in the scalp. There is a small group in the right groin. There are some erosions in the mouth.

DISCUSSION

DR. HERBERT RATTNER: I should consider pemphigus, provided a drug eruption can be ruled out. There were recently 3 Negroes with pemphigus in the Cook County Hospital.

DR. EDWARD A. OLIVER: I agree with Dr. Rattner's suggestion. Was the Nikolsky sign present?

OR. OLIVER S. ORMSBY: The lesions strongly suggest pemphigus. However, bullous erythema multiforme has to be considered. The lesions in the mouth are not painful as the lesions of pemphigus usually are. The disease is of short duration, and it will take time to decide its character.

DR. MICHAEL H. EBERT: I saw the patient for the first time the day before yesterday, and the appearance then was strikingly different from today. Originally the crop of lesions in the left genitofemoral region, particularly on the thigh, resembled herpes zoster. On the border there were discrete umbilicated lesions with some crusting. In the center they had coalesced. In addition, he had discrete bullous lesions on the face and some in the scalp. I thought at first sight the condition was a herpes zoster with a generalized eruption. The eruption had been present for thirteen days at that time, which was too long for herpes zoster. On examining him further I found bullae in the axillas and in the mouth. Then the usual triad was considered: toxic eruption, erythema multiforme and dermatitis herpetiformis. Dr. Otsuka made some sections rather hurriedly, which showed no indication of herpes simplex or of herpes zoster. The histologic picture would fit the other two disorders. The differential count of the circulating blood showed 2 per cent eosinophils. The smears of material from bullae had a high percentage of eosinophils, which might be suggestive of dermatitis herpetiformis.

His history is not of much value as far as drug taking is concerned. Basing my opinion on experience with Negro patients, I feel that the condition in this case may eventually prove to be pemphigus vulgaris.

Melanoma. Presented by DR. MICHAEL H. EBERT.

J. C., a white man aged 38, presents a new growth on the anterolateral surface of the right ankle. He has had a mole in this location all his life. About three or four years ago it became itchy and, he believes, more elevated. Seven weeks ago it was injured by a falling ladder; a crust formed and the lesion has increased in size.

There is a hemispherical firm mass 1 cm. in diameter. Half of the surface is eroded, and the other half is dull red. Around the tumor there is an irregular zone of black pigment varying from 1 to 5 mm. in width. There is also a uniform zone of erythema 1 cm. wide. Small glands are palpable in both groins.

DISCUSSION

DR. EDWARD A. OLIVER: I agree with the diagnosis. I believe that the lesion should be removed surgically immediately. I recently had a sad experience with a melanoma located in the left subcapsular region. The lesion had been quiescent for years, but the rubbing of the patient's suspenders produced some irritation and the lesion began to take on a malignant appearance. Because of the location it was treated intensively with radium and was not surgically excised. The patient remained well for a year. Then a metastatic lesion appeared in the left crural region and shortly after that a diffuse melanosis of the skin of the body together with great enlargement of the liver. He died just a few weeks ago.

DR. S. W. BECKER: I questioned the patient as to the nature of the mole. He said it was smooth and brown and recently became blue-black. From the experience of Kreibich and Bloch and from my own brief experience, it is the smooth brown mole that is dangerous, for it consists of an enormous number of monoblasts attached to the epithelium, sometimes several hundred times the normal number. According to many authorities, melanoma is apt to appear in this type of mole. I believe it should be excised widely and the defect filled in by a skin graft. Melanoma cells are radioresistant, and except in hopeless cases radiotherapy is not indicated.

Lymphoblastoma (Lymphosarcoma? Leukemia?). Presented by DR. HERBERT RATTNER and DR. MAURICE DORNE.

J. U., a white man aged 72, states that he was in good health until about nine weeks ago, when a walnut-sized lump developed on the roof of his mouth. Several days later there were generalized itching and intermittent headaches. About one week later numerous pea-sized nodules developed on the face, scalp, trunk and extremities. The itching subsided with the appearance of these nodules.

There were no other symptoms. About two or three weeks after its appearance the lump in the mouth became ulcerated.

There is a violaceous ulcerated infiltrated nodule the size of a half-dollar on the roof of the mouth, and there is a similar but nonulcerated nodule the size of a quarter on the left side of the forehead above the eye. There is a generalized eruption of pea-sized violaceous to light brownish nodules. The spleen is not palpable, but the liver is palpable. There is moderate generalized adenopathy. The prostate is enlarged.

The results of examinations of the blood made ten days apart were as follows:

	November 8	November 18
Hemoglobin	71 per cent	80 per cent
Erythrocytes	3,760,000	3,990,000
Leukocytes	4,900	2,950
Neutrophils	68 per cent	20 per cent
Lymphocytes	19 per cent	40 per cent
Monocytes	9 per cent	35 per cent
Basophils	1 per cent	0 per cent
Eosinophils	0 per cent	2 per cent
Metamyelocytes	2 per cent	2 per cent
Plasma cells	0 per cent	1 per cent

Sternal puncture revealed hyperplastic marrow and replacement of normal bone marrow by large numbers of early monocytoid cells.

The chemical examination of the blood and urinalysis gave normal results. The Wassermann reaction of the blood was negative. A roentgenogram of the chest and skull and a roentgenologic study of the gastrointestinal tract showed the structures to be normal.

The important histologic changes revealed in the section consisted of sharply outlined nests of infiltration, containing many monocytic cells, with absence of mitotic figures.

DISCUSSION

DR. FRANCIS E. SENEAR: It is worthy of comment that the condition apparently began on the palate. I believe that not all dermatologists would be apt to think of leukemia on seeing a single lesion in that location, though patients have been shown before this society with lesions of leukemia limited to the mucous membranes. Microscopic study would probably lead to the diagnosis.

DR. MARCUS R. CARO: I think that histologically lymphosarcoma can be ruled out. The infiltrate in the section is chiefly perivascular; there is absence of mitotic figures, and there are many monocytes present. I believe that the condition in this case is monocytic leukemia.

Grouped Comedos Following Herpes Zoster. Presented by DR. HERBERT RATTNER.

P. G., a man aged 60, from the Mandel Clinic of Michael Reese Hospital, states that in April he had herpes zoster, which involved the left supraorbital area and adjacent part of the scalp. He was treated with topical remedies, apparently calamine lotion. At no time did he apply any grease.

There are comedos in groups and some scars in the area that was involved with herpes zoster. There is some residual pain at the site.

DISCUSSION

DR. A. W. STILLIANS: One often sees milia, but I never saw comedos as a sequel of herpes zoster.

DR. HERBERT RATTNER: This case was presented simply as a clinical curiosity. I had never before encountered one like it.

Pityriasis Lichenoides Chronica. Presented by DR. MARTHE ERDOS-BROWN (by invitation) and DR. ARTHUR W. STILLIANS.

W. S., a man aged 24, born in Poland, presents an eruption of two years' duration on the flexor surfaces of the extremities and on the trunk, with a few lesions on the palms and soles. The face, scalp and neck are free. There is no eruption on the buccal mucosa. A geographic tongue is present.

The eruption consists of papules and macules varying in size from a few millimeters to 1 cm. in diameter, pink to yellowish red and more or less scaly. There is no confluence, and the lesions are scattered irregularly over the body There is no itching.

The patient was first seen on Aug. 12, 1941. The administration of solution of potassium arsenite U. S. P. has not influenced the eruption to date.

The Kahn reaction of the blood was negative.

Histologic examination, using hematoxylin and eosin, showed the demarcation between the epidermis and the cutis to be indistinct. The epidermis showed edema and moderate acanthosis. The corneum was nucleated. In the upper part of the cutis there were slight vascular dilatation and infiltration of lymphocytes.

This patient presents a classic picture of pityriasis lichenoides chronica.

A Case for Diagnosis (Pseudoepitheliomatous Hyperplasia? Benign Squamous Cell Tumor? Multiple Squamous Cell Epithelioma?). Presented by DR. EVANGELINE E. STENHOUSE (by invitation) and DR. S. W. BECKER.

A steel worker aged 36 has always had a dry scaly skin, worse in the winter. He had "eczema" in early childhood. Seven years before admission he had a "watery inflammation" of the left auricle, which healed in one week under treatment. Nine years before observation he noted a warty growth on the inside of the left auricle just posterior to the external auditory meatus. The lesion enlarged, with drainage of pus and formation of sinuses. During the last four years he has had several growths on his face, some of which subsided leaving pitted scars. The lesion on the nostril has been present for about six weeks. He had three roentgen ray exposures one year before observation. The patient had a productive cough for about six years with occasional slight hemoptysis.

The left auricle is greatly swollen and deformed and shows many sinuses from which pus is discharging, some of which extend completely through the auricle. Anteriorly and posteriorly there are ulcers with elevated borders. There are many vegetations within the external ear. At the edge of the left nostril, at the right internal canthus and below the left oral commissure are elevated tumors 0.5 to 0.75 cm. in diameter with elevated borders. On various parts of the face are depressed atrophic scars 0.5 to 0.75 cm. in diameter with considerable destruction of tissue.

Physical examination reveals a rather thin person. The pupils are irregular and do not react to light or in accommodation. The gag reflex, biceps reflex and knee and ankle jerks cannot be obtained. Examination in the chest clinic revealed the lungs to be clear on palpation, percussion and auscultation. A roentgenogram of the chest showed accentuation of pulmonary marking, especially the bronchovascular trunks into the bases of the lung. The findings were interpreted as suggestive of bronchiectasis. Neurologic examination revealed probable tabes dorsalis. The spinal fluid was not examined because of the infection in the ear. Examination in the ophthalmic clinic revealed probable Adie's syndrome.

The Kolmer and Kahn reactions of the blood serum were negative on three occasions. The urine was normal. A blood cell count showed 19,200 leukocytes and 4,060,000 erythrocytes, with a differential distribution of 82 per cent polymorphonuclear leukocytes, 5 per cent small lymphocytes, 3 per cent mononuclear leukocytes, 9 per cent eosinophilic leukocytes and 1 per cent basophils. There was 14.6 Gm. of hemoglobin per hundred cubic centimeters of blood. Microscopic examination of pus from an ulcer on the left ear showed many pus cells but no fungi. No enlarged lymph nodes could be palpated. Cultures of pus from the left

ear showed streptococci, staphylococci and gram-negative rods. Later cultures grown on Sabouraud's medium, blood agar, veal infusion agar slants and Rosenau's brain broth and deep inoculations in dextrose veal infusion agar all showed Pseudonomas pyocyanea. All except Sabouraud's medium showed gram-positive diphtheroid bacilli. No fungi were found on Sabouraud's medium.

Microscopic examination of a section from the center of the elevated portion of the ear showed considerable crusting with thickened parakeratotic stratum corneum. The epidermis had proliferated and extended deeply in the form of normal acanthosis except that some of the deeper processes appeared as separate islands. There were occasional pearls or pseudopearls in the deeper processes. In places there was considerable infiltrate consisting of round cells and some plasma cells. A section from the posterior border at the junction with the normal skin showed penetration of the epithelium into the dermis with pearl formation in separated islands. Section removed at the nostril showed even more pronounced penetration into the dermis with the formation of many pearls. Section removed at the left inner canthus showed penetration into the dermis with much hyperkeratosis and many pearls. There was only slight anaplasia, and practically no mitotic figures were seen.

In view of the probable diagnosis of squamous cell epithelioma the patient was given roentgen therapy to the left ear. Large doses of iodides were given daily by the intravenous route in view of the diagnosis of tabes dorsalis and the possibility of mycotic infection.

DISCUSSION

DR. M. H. EBERT: I think there are on record cases of multiple epitheliomas associated with congenital deformities of the central nervous system. It might be well to investigate the case with that in mind rather than the possibility of tabes.

DR. S. W. BECKER: In line with Dr. Ebert's suggestion, this man does have Adie's syndrome and other neurologic findings suggestive of tabes dorsalis. It is not often that one sees tumors which on section seem to be squamous cell epithelioma but clinically do not follow the usual course of squamous cell tumors. Dr. Poth reported the case of a man on the back of whose hand tumors would develop on exposure to the sun; when he stayed out of the sun they would undergo involution without leaving scars (Poth, D. O.: Tumor-like Keratoses, ARCH. DERMAT. & SYPH. **39**:228-239 [Feb.] 1939). Dr. Flory, working with tobacco tars, which were applied to rabbits' ears (Flory, C.: Production of Tumors by Tobacco Tars, *Cancer Research* **1**:262 [April] 1941), was able to produce squamous cell epithelioma at times even with cellular masses in the lymphatics. After application of the tobacco tar was discontinued the tumors would regress entirely.

We considered a great many possibilities in this case. If the condition is a squamous cell epithelioma it has run an unusual course. If it is a benign squamous cell tumor it is also unusual.

NEW YORK DERMATOLOGICAL SOCIETY

J. GARDNER HOPKINS, M.D., *President*

A. BENSON CANNON, M.D., *Secretary*

Nov. 25, 1941

Dermatitis Herpetiformis. Presented by DR. J. GARDNER HOPKINS.

T. M., a man aged 45, presented for Dr. George Heustis Fondé, has had for two months a generalized eruption, most profuse on the backs of the shoulders, the extensor surfaces of the arms and the buttocks. The eruption is made up of red scaling patches in which are groups of papules and an occasional bulla, 0.5 cm. in diameter.

The results of general physical examination and numerous laboratory studies were normal except that abscessed teeth were found. These were removed, without any effect on the eruption.

With the patient under treatment with sulfathiazole for eight days the eruption cleared almost completely, but the administration of this drug had to be discontinued because the patient felt ill and lost weight.

The case is presented for suggestions for therapy.

DISCUSSION

DR. A. BENSON CANNON: The only cases of dermatitis herpetiformis that I have observed in which there was permanent cure have been those in which a focus of infection was found and eliminated. I recall 3 cases in which there were spectacular cures, in 2 after extraction of abscessed teeth and in the third after the cure of pyelonephrosis. In each case, improvement was noticed immediately after the removal of the infected focus, and within a few weeks all the lesions and symptoms had disappeared. The patients remained well.

DR. FRED WISE: I have obtained good results in the treatment of Duhring's disease with a combination of injections of 2 per cent solution of sodium arsenate, autohemotherapy and roentgen irradiation.

DR. FRANK C. COMBES: Arsenic is the best treatment there is now for this disease, but I think its use is too empiric. Therefore, I should follow Dr. Cannon's suggestion and search for foci of infection. In the absence of any demonstrable focus of infection, I think good results can be obtained by the use of sulfanilamide or one of its derivatives. In 1 case in which there was spectacular improvement Dr. Costello administered sulfapyridine.

DR. J. GARDNER HOPKINS: How do you feel about using roentgen rays?

DR. FRANK C. COMBES: Roentgen rays in some cases will relieve itching, but I do not think that in cases of such chronicity it is advisable to use them.

DR. R. H. RULISON: I cleared up the condition in 1 patient with sulfanilamide, but the eruption recurred and later sulfanilamide had no effect. I think that roentgen rays often give great relief and even cause a remission, but of course they will not cure the condition.

DR. PAUL E. BECHET: The eruptions of Dr. Hopkins' patient and mine present much the same degree of severity. In cases of this disease I have obtained improvement and considerable relief from pruritus by giving intramusclar injections of whole blood twice a week.

DR. HOWARD FOX: One frequently hears of sporadic cases in which this condition was cleared up by sulfanilamide or one of its derivatives. Dr. Costello has had 2 such cases; one of his patients remained well at least a year. From other cases that have been reported, it seems necessary to continue to give a maintenance dose of the drug, for otherwise a relapse will take place. It is certainly not a specific cure as a rule.

DR. EUGENE F. TRAUB: I also had several cases in which the drugs of this group caused some improvement in the lesions. In 1 case there has been improvement with sulfadiazine (2-[paraaminobenzenesulfonamido]-pyrimidine), a drug which I thought was safer to use. Dr. Ormsby has recommended calcium thiosulfate as being of value for this condition. Sometimes generalized ultraviolet irradiation is of greater help than treatment with roentgen rays in relieving the itching.

DR. A. BENSON CANNON: Fever therapy is sometimes beneficial in dermatitis herpetiformis.

Lichen Sclerosus et Atrophicus (Hallopeau). Presented by DR. PAUL E. BECHET.

A. M., a woman aged 56, presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, stated that her eruption

had been present for two years. It began on the flexor surfaces of the forearms and wrists and later appeared on the feet, ankles and dorsal surface of the left hand. These lesions never itched, and there are no scratch marks.

On inspection polygonal to round, lentil-sized, raised, chalky white to ivory-colored, indurated papules with a tendency toward grouping are observed. Dark gray horny comedo-like plugs are present on several of the papules and also in a few of the deep punched-out scars.

Routine laboratory tests gave normal results.

Histologic examination showed that throughout the upper part of the cutis there was considerable edema with areas of hemogenization of tissue. The latter took a brighter stain. Beneath this there was a moderate small round cell infiltration somewhat in bandlike fashion. The overlying epidermis was thin and flat, and the basal cell margin was washed out in some areas. The histologic diagnosis was lichen sclerosus et atrophicus.

DISCUSSION

DR. A. BENSON CANNON: I think that the location and the shiny, umbilicated, annular lesions with atrophy are typical of lichen planus atrophicus.

DR. EDWARD R. MALONEY: I do not think the diagnosis presented is correct. I should call this condition lichen planus atrophicus. There are undoubtedly lichen-planus-like lesions which enlarge and finally disappear, leaving atrophic white spots. I think lichen planus atrophicus is the better diagnosis, leaving out the term sclerosus, unless it has been demonstrated histologically that sclerosis is present.

DR. FRED WISE: Lichen sclerosus et atrophicus of Hallopeau is devoid of lichen planus lesions in all stages of the eruption. The characteristic lesion is an indurated papule which has a central cornified dark plug or a papule with a central depression, representing the site of previously existing plug which had either dropped out or had disappeared as a result of involution of the papule itself. The late stage consists of a white or ivory-colored, smooth, flat, indurated and sclerotic papule. These sclerotic papules become fused, resulting in plaques resembling circumscribed scleroderma. On the other hand, the papules of lichen planus atrophicus exhibit evidence of an atrophic process in the earliest stages of their evolution; the papules show a central delling, but no plugs as in Hallopeau's disease.

DR. EDWARD R. MALONEY: I agree with Dr. Wise. I thought this condition was lichen planus atrophicus because there are definite lichen planus lesions in the lichen planus areas. The lesions of the other disease are not in the lichen planus areas and are not lesions of lichen planus.

DR. R. H. RULISON: The patient told me there had never been any redness or itching or any elevation of these patches. I am inclined to agree with the diagnosis as presented.

DR. FRANK C. COMBES: In spite of all that has been said, I still agree with the original diagnosis. The location is in favor of lichen planus, there is no doubt about that, and the histologic structure is suggestive of lichen planus. The absence of itching is against it, and I could see no typical lichen planus papules. She has atrophic and hypertrophic lesions which are flesh colored, almost white. In a few of the lesions there are follicular puncta such as are seen in Hallopeau's type of lichen sclerosus.

DR. GEORGE C. ANDREWS: I believe the diagnosis in this case is lichen planus atrophicus for the reasons already mentioned by Dr. Wise and Dr. Maloney and, in addition, because of the fact that in the microscopic section the infiltration is rather deep. The section is poorly stained, but nevertheless one can see a deep infiltration in some areas and there is no sclerosis.

DR. EUGENE F. TRAUB: When I first saw this patient I thought there was very little doubt that this condition was lichen planus atrophicus for the reasons stated by Dr. Wise and Dr. Maloney, but the lesions on the dorsum of the foot

looked more like lichen sclerosus et atrophicus. Under the microscope one can see the little keratotic plugs which I think would fit in with the diagnosis of lichen sclerosus et atrophicus, although taken as a whole the histologic picture seems indecisive.

DR. PAUL E. BECHET: The clinical evidence is in favor of the diagnosis, and the clinical picture agrees with the classic description of lichen sclerosus et atrophicus (Hallopeau), namely, polygonal, flat-topped, ivory and mother-of-pearl papules, both discrete and grouped. In a good light, dark horny comedo-like plugs can be discerned on several of the papules, and deep punched-out scarring is also present. The histologic report is lichen sclerosus et atrophicus. There is no itching, and there are no scratch marks.

Rosacea-Like Tuberculid of Lewandowsky. Presented by DR. GEORGE C. ANDREWS.

C. R. C., a man aged 25, was first seen about eight months ago with erythematopapular, crusted, discrete lesions on the cheeks. Some of the individual lesions are rather yellowish brown and vary in size from that of a pinhead to that of a split pea. The right side of the face has shown a little more eruption than the left. The condition has remained localized to these areas and has shown practically no change since the patient was observed last April.

During childhood the patient had some swollen glands in his neck and had an elevated temperature for some time. A diagnosis of tuberculous adenitis was made at that time. In more recent years he has been closely associated with a cousin who died of "galloping consumption." There is nothing else in the past history of significance. The patient has had no sickness in his life except the usual diseases of childhood. There is no history of previous disease of the skin except interdigital dermatophytosis. A recent physical examination by an internist failed to disclose anything of significance except for the eruption.

A tuberculin test with a 1:1,000,000 dilution of old tuberculin elicited a positive reaction consisting of an erythematous indurated reaction 2 cm. in diameter. A 1:10,000,000 dilution of old tuberculin elicited a positive cutaneous reaction which was somewhat smaller. A complete blood count and urinalysis showed normal results.

Histopathologic examination by Dr. G. F. Machacek was reported as follows: "A small piece of skin was examined microscopically after sectioning. It was found that hyperkeratosis and localized parakeratosis were present, as well as edema and moderate acanthosis. Numerous pilosebaceous organs were present. The corium was edematous; within it a granulomatous infiltration was seen. Some distance from this granuloma, which showed no characteristic changes, a tiny tubercle was discovered containing numerous giant cells. No acid-fast organisms were seen. The lesion, although not absolutely characteristic for tuberculosis, was probably a rosacea-like tuberculid."

Treatment has consisted of injections of a 1:1,000,000 dilution of old tuberculin and gold sodium thiosulfate (ten injections of 0.025 Gm. each), bismuth subsalicylate, neoarsphenamine, vitamin A, nicotinic acid and sulfathiazole (2-[para-aminobenzenesulfonamido]-thiazole) by mouth. Several fractional doses of roentgen rays (75 r) were given to the affected areas, and a sulfur lotion and alibour water (water containing zinc and copper sulfates) were prescribed. The tuberculin therapy has on occasions produced some slight temporary benefit. None of the other treatment has apparently been of any benefit, and the condition as seen at this time is much the same as it was when the patient was first observed eight months ago.

DISCUSSION

DR. EUGENE F. TRAUB: I agree with the diagnosis. If ultraviolet irradiation has not been used, I certainly suggest its trial. It seems to help at times.

DR. GEORGE C. ANDREWS: Ultraviolet irradiation has been tried.

DR. PAUL E. BECHET: Dr. Andrews' patient shows no rosacea or telangiectasia. The lesions are indistinguishable from those of lupus miliaris disseminnatus

faciei. I have long entertained doubt as to the advisability from a clinical standpoint of considering rosacea-like tuberculid of Lewandowsky a distinct entity. I have seen so many examples of typical folliculitis, acnitis and lupus miliaris disseminatus faciei designated as Lewandowsky's disease, that I should be in favor of eliminating that name from dermatologic nomenclature, despite the fact that telangiectasia, hyperemia and absence of necrosis are advanced as differential points in the diagnosis.

DR. FRANK C. COMBES: I think the condition in this case is typical clinically and histologically, but it is atypical in its response to treatment. I cannot offer any suggestion unless it is to persist in the use of gold sodium thiosulfate with large doses of ascorbic acid.

DR. FRED WISE: Four or 5 patients treated at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital in the past few years responded quickly to injections of a gold compound. I should increase the dose to 75 or 100 mg. for this patient.

DR. J. FRANK FRASER: I think this condition is Lewandowsky's tuberculid. The distribution is characteristic, and the histologic picture, although not typical, in my opinion harmonizes with that diagnosis.

DR. EDWARD R. MALONEY: I do not like the name rosacea-like tuberculid because, as in this particular case and as Dr. Bechet brought out, the lesions are not in the typical rosacea area. They are more on the jaws. The condition is a tuberculid, but I do not see why it should be given a particular name such as rosacea-like tuberculid. I think such eruptions should be called tuberculosis or tuberculid. However, as rosacea-like tuberculid is understood today, I think that is the correct diagnosis in this case.

DR. J. GARDNER HOPKINS: One does not very often see telangiectases in conditions of this kind.

DR. FRANK C. COMBES: There is erythema in such conditions.

DR. J. GARDNER HOPKINS: In view of the good results I have seen at Vanderbilt Clinic with tuberculin in cases of this kind, I think I should follow that up, especially as this patient is so extremely sensitive to tuberculin.

DR. GEORGE C. ANDREWS: I have had the same experience as Dr. Wise, observing that gold sodium thiosulfate is effective as a rule in these cases. I had to stop giving the gold compound in this case because of the exfoliative dermatitis on the palms. The ascorbic acid, however, I should like to give him, and I shall also follow Dr. Traub's suggestion of generalized ultraviolet irradiation.

Pellagra (with Flexural Lesions). Presented by DR. FRANK C. COMBES.

H. J., a Negress aged 31, was previously presented before the Metropolitan Dermatological Society on Nov. 17, 1941 (ARCH. DERMAT. & SYPH., to be published).

The patient had for several months taken spirituous liquors to the exclusion of food. Three weeks ago evidences of vitamin B deficiency developed. These at present consist of stomatitis, cheilitis, glossitis, redness, scaling, pigmentation and excoriation on the backs of her hands and other lesions on her body. The latter are located beneath her breasts and in the genitoanal region. Here she presents sharply defined, eroded, oozing patches, bilaterally symmetric, extending from the sacral region downward and anteriorly on the thighs in the perineal region. They extend for about 5 cm. on either side of the midline. Similar lesions are present beneath her breasts.

She has shown remarkable improvement within three days from administration of 300 mg. of nicotinic acid daily. Examinations for fungi were negative.

DISCUSSION

DR. EUGENE F. TRAUB: The condition in this case is a typical example of pellagra, but at the same time the lesions must be regarded as somewhat unusual.

DR. HOWARD FOX: The lesions look like those of pellagra. They are in an unusual location. They suggest psoriasis or a mycotic infection which has been treated, but as the patient has improved under nicotitic acid therapy, I think there is no doubt about the diagnosis of pellagra.

DR. A. BENSON CANNON: I think one not infrequently finds lesions of pellagra on the flexor surfaces, in the groins, in the crotch and between the folds of the buttocks and sometimes in the axillas, between the toes and on the fronts of the ankles, as well as on the back of the neck. I have observed a great many cases of pellagra in the South, and I can recall several in which there were macerated, verrucous-like, sharply marginated cutaneous lesions, as in this case.

DR. FRED WISE: I should like to ask Dr. Hopkins whether in an eruption of this type the histologic examination would be of value in arriving at a diagnosis of pellagra.

DR. J. GARDNER HOPKINS: The histologic examination is of little value in making the diagnosis. The diagnosis of pellagra rests on the response to treatment with nicotinic acid. It was my impression that this intergluteal lesion was characteristic. Some cases have been described in which intergluteal and vaginal lesions were the most prominent ones. The general impression is that the lesions occur in areas of friction or of exposure to the sun. If the patient had a polyneuritis she doubtless had not only a nicotinic acid deficiency but also a vitamin B_1 deficiency. That seems frequent in the experience of those who are studying pellagra. Most of the patients show other symptoms which can be cleared up by the administration of liver and other mixed vitamins, but if one gives nicotinic acid alone, in most of the cases other deficiencies show up requiring riboflavin or vitamin B_1 to clear them up.

DR. HOWARD FOX: At the first Pellagra Conference, in 1908 in Columbia, S. C., I observed many cases and have encountered a reasonable number since then at Bellevue Hospital. I still think the location on the flexor surface is unusual. Lesions under the breasts and in the intergluteal region are also not common.

DR. EDWARD R. MALONEY: May I add something in corroboration of what Dr. Fox has said? Of course, at Bellevue Hospital a great many patients with alcoholic pseudopellagra are seen, and they do not show these intertriginous lesions. My impression is that the intertriginous lesions are rather rare. I cannot remember having seen many of them.

DR. GEORGE C. ANDREWS: Is it not true that lesions in the vagina and in the mouth are common in true pellagra?

DR. FRANK C. COMBES: The lesions in the intergluteal region seem to have aroused a great deal of comment. I have not encountered so many cases of pellagra, but I know that Edward Jenner Wood in his report of the North Carolina Pellagra Commission covering thousands of cases never reported one in which there was a lesion in this exact location.

Xanthoma Tuberosum with Involvement of the Palms. Presented by DR. FRED WISE.

S. G., a woman aged 48, referred by Dr. Charles R. Rein, registered at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Nov. 3, 1941, with complaints of a multiplicity of vague and more definite subjective symptoms referable to general medical and neurologic disturbances of two years' duration. She had typhus fever twenty years ago. Three months ago she noticed a yellowish discoloration of the palms. She gives no history of cardiac disease or jaundice. Until ten weeks ago her diet consisted of excessive amounts of bread and butter, cheese, alligator pears, squash, carrots and other yellow vegetables. She complains particularly of dizziness, heaviness and dulness in the left side of the head, dryness of the throat, blurred vision and stiffness of the left arm and leg. The pain in the leg seems to follow the dis-

tribution of the sciatic nerve and occurs in the form of cramps. The pains in the head are rather frequent, occurring about every half-hour and lasting for about fifteen minutes. She has been taking petrolagar as a laxative.

All the creases in the palms, including part of those on the left wrist, are entirely filled with yellowish streaks which are smooth, not raised, and look as if they were colored with a yellow dye. There are similar yellowish pigmented, ill defined, dime-sized areas in the intergidital spaces between the index and middle fingers. There were three small pinhead–sized yellowish nodules on the extensor surface of the left elbow, which were removed for histologic study. There are no other lesions on the integument or on the oral mucosae. The scleras are clear.

The routine laboratory data, including results of chemical examination of the blood, were normal except for a leukocyte count of 12,500. Special chemical examination of the blood serum gave the following results: total protein, 9.2 per cent (normal 6 to 8); albumin 3.3 per cent (normal 4 to 5), and globulin, 5.9 per cent (normal 2 to 3), with a ratio of 0.6 (normal 1.6-2.0: 1). The cholesterol content of the blood on October 13 at the Mount Sinai Hospital was 875 mg. per hundred cubic centimeters (normal 175 to 125 mg.). The values for the lipid partition of the blood serum on November 14 at the New York Post-Graduate Hospital were as follows: total lipids, 1,051 mg. per hundred cubic centimeters (normal 500 to 700); fatty acids, 401 mg. (normal 200 to 420); lipid phosphorus, 15.7 mg. (normal 7 to 14); cholesterol, 630 mg. (normal 160 to 230); cholesterol esters, 385 mg. (normal 100 to 150); ratio esters to total cholesterol, 61 per cent. The diminution in the cholesterol content of the blood is due to the fat-free cholesterol-free diet on which the patient has been since November 3.

The sedimentation rate (Westergren method) of the blood was 10 mm. in one hour (normal, 18 mm.). The dextrose tolerance, the carotene content of the blood, the icteric index, the basal metabolic rate and an electroencephalogram (Dr. Pacella) were normal. The electrocardiographic examination showed left axis deviation and a T wave of low voltage in lead IV. Oral cholecystography showed good filling and emptying of the gallbladder. There was no evidence of gallstones. A roentgenogram of the pituitary showed the sella turcica to be normal in size and shape. Physicians at the Mount Sinai Hospital were unable to demonstrate any evidence of organic disease which might contribute to the production of the hypercholesteremia, but they suggested that "a xanthomatosis of this type might be accompanied by extensive arterial changes."

A histologic section taken from the small nodules on the left elbow and examined by Dr. Charles F. Sims was diagnosed as xanthoma with the following description: "The epidermis presented no noteworthy changes. In the upper portion of the cutis there were several small masses of cells which on high power presented a foamy cytoplasm and a hyperchromatic nucleus. There was some interstitial edema in the upper part of the cutis."

The patient has been given a cholesterol-free diet.

DISCUSSION

DR. EDWARD R. MALONEY: I agree with the diagnosis. I should like to ask Dr. Wise, however, whether this deposit of xanthomatous material in the creases of the palms is not rare.

DR. EUGENE F. TRAUB: The lesion on the elbow was excised to relieve the pain and discomfort of which the patient complained. The lesion is gone now, but she still complains of pain and discomfort at that site.

DR. J. GARDNER HOPKINS: This woman showed a moderate arcus senilis, such as most patients with this condition have. I wonder how much of her internal symptoms can be correlated with her xanthomatosis. Of course such patients do get internal deposits of xanthomatous material.

DR. FRED WISE: The patient had had one of the rather large lesions on the elbow excised, and the site healed without keloid formation or return of the xanthoma. So far there has been no tendency toward recurrence of the lesion at that site.

Keratosis Blennorrhagica. Presented by DR. FRANK C. COMBES.

C. G., a Negro aged 23, now calling himself U. S. G., whose case was reported previously (Combes, F. C.; Dietrich, C., and Cohen, J.: Keratosis Blennorrhagica, *J. A. M. A.* **114**:2078 [May 25] 1940), was admitted with a recurrence more extensive than his original attack but not accompanied by as severe constitutional symptoms.

His present illness began about three months ago with polyarthritis, a generalized scaly dermatitis appearing three weeks ago. The latter is identical with that previously described, but in addition he has many lesions on the trunk and the arms are literally covered with the eruption. Cultures of material from his joints and from the prostate were negative for gonococci. Smears from beneath the scales showed many gram-negative diplococci, none of which was intracellular. A blood culture was negative. Gonococcus filtrate given intracutaneously elicited a strongly positive reaction. He is at present receiving sulfathiazole (2-[para-aminobenzenesulfonamido]-thiazole), 1 Gm. every four hours, with no improvement.

DISCUSSION

DR. A. BENSON CANNON: The lesions are unusually extensive, and I should think that properly regulated fever treatment would be curative.

DR. HOWARD FOX: This patient presents undoubtedly the most extensive example of keratosis blennorrhagica I have ever seen. I agree with the statement that it is extremely rare to find gonococci in the cutaneous lesions. I am surprised that this condition did not improve with fever therapy. I understand that the arthritis cleared up but that the cutaneous lesions were not affected.

DR. GEORGE C. ANDREWS: There have been reports in this country of the finding of gonococci in the cutaneous lesions. In my textbook there is a reference to at least one of these reports.

DR. FRANK C. COMBES: The condition cleared up before with fever therapy, but this time it did not.

DR. EUGENE F. TRAUB: I should like to comment on the lesions across the bridge of the nose, which strongly suggest lupus erythematosus. I have always looked on lupus erythematosus as a symptom of bacterial allergy; therefore there is no reason why any type of bacterial infection cannot produce a lupus-erythematosus-like type of lesion. I believe that is what this patient has.

DR. J. GARDNER HOPKINS: It is interesting that this eruption occurs so rarely in gonorrhea. I wonder if it can be shown that persons with this condition have a cutaneous allergy with extracts of the organisms. My impression was like that of Dr. Andrews, that there had been a number of reports of the finding of gonococci in cutaneous lesions of this kind. Most of the gonococci have been identified morphologically. Bacteriologists now have methods of growing the gonococcus which recover it when it is difficult to identify in smear.

DR. GEORGE C. ANDREWS: Is the new medium to which you refer brain broth?

DR. J. GARDNER HOPKINS: I do not know what it is.

DR. A. BENSON CANNON: I recall that years ago Dr. Fordyce had a case of gonorrheal ulcers in which isolation and culture of gonococci from the cutaneous lesions were reported.

DR. FRANK C. COMBES: As to fever therapy, the patient responded in the previous attack, almost miraculously. After the first treatment his arthritis improved, and the cutaneous lesions disappeared after about six treatments. As for the presence of gonococci, I did not observe any on the previous admission, but this time he was admitted to the medical service because of arthritis. Gram-negative diplococci were found, but they were not intracellular. I repeated the investigation, but I was not satisfied with the staining. This could be explained on the basis of a change in habitat of the organism, causing a change in staining properties. The patient is sensitive to gonococcus filtrate and at present is being treated with it. On this admission he got worse with the fever therapy given in the medical service, but I think it will be tried again in my service. I do not know why he should not respond to it this time as he did before.

Papulonecrotic Tuberculid (Lesions on the Palms). Presented by Dr. Frank C. Combes.

E. B., a man aged 60, presents an eruption more or less limited to his extremities, particularly the extensor surfaces, consisting of necrotic papules in various stages of evolution. On each palm are approximately a dozen lesions. The eruption is of five weeks' duration. A similar eruption several years ago responded promptly to injections of neoarsphenamine. In 1926 the patient had active pulmonary tuberculosis. His tuberculin reaction is positive with a dilution of 1 : 1,000,000.

DISCUSSION

Dr. A. Benson Cannon: I cannot recall ever having seen a vesiculopustular eruption occurring on the palms in a case of papulonecrotic tuberculid, nor should I think that one would be apt to find this type of lesion on the extensor surface in the disease. However, if Dr. Combes has studied the case clinically and has found the condition histologically to be papulonecrotic tuberculid, I should think that one would agree with his diagnosis.

Dr. Edward R. Maloney: I think that is about as good a diagnosis as one can make in this case. It fits in that group. As Dr. Cannon said, many of the lesions are in unusual locations, such as the palms, and some of them do not look exactly like the individual lesions of papulonecrotic tuberculid. In general, however, there are enough of them which have the characteristic appearance of papulonecrotic tuberculid and run the characteristic course of that disease, leaving the pitted scars to make that diagnosis.

Dr. Fred Wise: I agree with the diagnosis as presented.

Dr. George C. Andrews: I was interested in the distribution of the lesions on the palm in relation to that of pustular bacterid. I am always interested in the reasons why lesions occur in a particular location.

Dr. Howard Fox: I agree with the diagnosis and agree with the other speakers that it is unusual to see so many lesions or even to see a few lesions on the palms. I am sure I have seen an occasional one on the palmar surface of the fingers. I do not agree with the statement that this disease does not occur after the age of 30, because one of the most profuse eruptions I have ever seen occurred in a woman of about 50, the superintendent of a large hospital. I can also recall a patient aged 44, the wife of a doctor, who had an extensive eruption.

Dr. Eugene F. Traub: In the face of all the agreement with this diagnosis, I hesitate to disagree, but the points which struck me are that this patient is 61 years of age and that the eruption came on suddenly and simultaneously in all areas only five weeks ago. It began as a vesicle, not as a hard papule. The lesion goes through a hemorrhagic stage. Some of the vesicles are infected, some are scaly and some terminate in rather deep necrosis. If a dermatophytosis and an id can be excluded, which I believe will prove likely, I am certain this condition is an example of parapsoriasis varioliformis acuta. Further observations, I am sure, will prove that it is not a papulonecrotic tuberculid.

Dr. Frank C. Combes: Dr. Traub's suggestion of parapsoriasis varioliformis can be answered, I think, by the fact that this patient has only the necrotic lesions. I do not see any other lesions on which one could make the diagnosis of parapsoriasis. This man had his initial attack of pulmonary tuberculosis when he was over 40 years of age, and that might account for the late appearance of these lesions. I do not know of any way of clinical differentiation between the lesions of papulonecrotic tuberculid and those of parapsoriasis varioliformis. The patient had one previous crop of lesions, which responded promptly to neoarsphenamine.

Dr. George C. Andrews: Is it not true that in parapsoriasis varioliformis there are polymorphic lesions in all stages of development?

Poikilodermatomyositis. Presented by Dr. Fred Wise.

S. K., a man aged 52, referred by Dr. G. Rubin, registered at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Oct. 28, 1941, complaining of cutaneous lesions, swelling of the throat, numbness of the fingers and painful muscles. For the past seventeen years he has been working as a laborer handling asphalt and tar in paving the streets. He has always been in good health until the present illness, which is of three months' duration. He had a severe sunburn on the face and scalp in July of this year, which was followed a month later by itching. The redness of the face has persisted. About three weeks ago pains developed in the shoulders and upper limbs. During the past two weeks the muscles of the nates and the thighs became similarly affected. The hair of the scalp has been falling out for a month.

The patient complains of pain in the muscles; he is unable to use his hands and arms and walks with difficulty. The scalp presents areas of diffuse erythema with thinning of the hair, which is fine and silky. The face, especially the central portion, and the eyelids are edematous and dusky red but not scaly. The tongue is heavily coated. He is unable to open the mouth widely because of the pain and swelling in the cheeks. There is a moderate leukoplakia in the right oral mucosa near the commissure of the mouth. The palate and the pharynx are injected and the gums pyorrheic. There is a diffuse swelling of both upper extremities, most pronounced on the dorsal surfaces of the hands, so that he is obliged to hold his hands in a semiflexed position. On the extensor surfaces of both elbows are ill defined patches which are purplish red and present areas of thinning, wrinkling and telangiectasia. The extensor surfaces of the fingers also present ill defined areas of telangiectasia with some small depigmented, sclerodermatous areas. On the outer and inner surfaces of the upper parts of the thighs are two fairly well defined, smooth, erythematous, telangiectatic patches arranged longitudinally, 7 inches (17.5 cm.) in length and 3 inches (7.5 cm.) in width. These patches are purplish red and nonscaly and interspersed with irregular, match head–sized to pea-sized, white, depigmented areas, giving a reticulated appearance. These patches fade only very slightly on moderate pressure. There are similar but smaller patches on the extensor surfaces of the thighs. The affected muscles and the cutaneous manifestations show almost a perfect symmetry in distribution, size and appearance. The involved muscles are tender but do not apparently show any disturbance in nerve sensitivity, as evidenced by examination with a point and hub of a needle.

Except for the muscle disturbance, the patient does not give evidence of any pathologic disturbances in any other organ. He is of strong physique and has no fever. The lungs are clear and the heart sounds of good quality. The blood pressure is 135 systolic and 50 diastolic for the left arm and 100 and 50 respectively for the right arm.

The results of routine laboratory tests were normal except for an erythrocyte count of 3,650,000 and 9 per cent band forms. Reactions to intracutaneous tuberculin tests with old tuberculin in dilutions as low as 1 : 10,000 were negative.

A histologic section from a lesion on the extensor surface of the upper part of the right arm, examined by Dr. Charles F. Sims, was described as follows: "The epidermis was thinned, and the rete pegs were short and difficult to distinguish. In some parts of the section the prickle cells in the lower part of the rete presented rather large nuclei with intense-staining chromatin. Beneath these areas the basal cells appeared to be greatly disorganized. The entire cutis presented a decided interstitial and parenchymatous edema, most apparent in the papillary and subpapillary zones. In these zones there was a pronounced granular degeneration in several parts of the section. Some basophilic strands were noted scattered throughout the upper and middle parts of the cutis. The blood vessels were dilated throughout the section, with their walls edematous, presenting a frayed appearance. In the subepidemic zone there were several areas in which telangiectatic vessels were to be seen. Surrounding the vessels the collagen framework presented a decided parenchymatous edema. An exceedingly sparse, small round and wandering connective tissue cell infiltration was noted in the vicinity

of some of the vessels. The elastic tissue was apparently little disturbed except for some slight fragmentation in parts of the upper portion of the cutis. The adnexa were apparently unaffected. The observations were suggestive of an acute diffuse lupus erythematosus, but in view of the clinical history of muscle swelling and tenderness, another biopsy of tissue, including muscle, is advisable."

DISCUSSION

DR. A. BENSON CANNON: I agree with the diagnosis and think the case is a most unusual one.

DR. EDWARD R. MALONEY: I also agree with the diagnosis in this interesting case. Dr. Wise seems to have covered the ground well in his investigation.

DR. J. GARDNER HOPKINS: The lesions on the thighs certainly looked like poikiloderma, and there were atrophy and also induration of the muscles. The involvement of the face and muscles of the jaw struck me as unusual, but I was interested in the oral sepsis, which has been described in a number of the cases; in several of them there was severe exacerbation on the removal of infected teeth. At the same time oral sepsis is so common that some physicians have doubted that it is a causative factor in the disease. I should like to ask whether this man has had any febrile attacks.

DR. FRED WISE: I should like to ask Dr. Hopkins, after what he has said, whether any attempt should be made to clean up the mouth.

DR. J. GARDNER HOPKINS: I had a patient who showed an exacerbation after the removal of infected teeth, but I think that should be prefaced with what has already been said about there being no treatment for this disease at present. I should make an attempt for a sick patient to remove the infected teeth, but I should have him in the hospital at the time.

DR. GEORGE C. ANDREWS: I presented a case like this last year (ARCH. DERMAT. & SYPH. **43**:1035 [June] 1941), that of a young woman in whom this condition came on after an artificial menopause which was due to roentgen ray exposures of the ovary and pituitary gland. This condition came on about six weeks later. She is still alive but is very sick.

Disseminated Sarcoidosis, Treated with Diphtheria Toxoid. Presented by DR. FRED WISE.

J. M., a man aged 26, registered at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Sept. 2, 1941, presenting disseminated lesions. He first noticed a swelling in the inguinal region about a year ago. In January 1941 "pimples" the size of a pea developed on both shoulders. They continued to enlarge. They then appeared on the left side of the neck, in the malar and frontal regions and, a few months ago, on the arms and back. They have never regressed. The family history is irrelevant. The patient has been having supraorbital dull headaches for many years at intervals of about twice a week, which last for a day or longer. He has otherwise been in good health, working long hours on two jobs.

The patient presents roughly symmetric, generalized, painless growths on the face, trunk and upper and lower limbs, with a predominance on the extensor surfaces, especially on the upper part of the back and shoulders. The growths consist of (1) pea-sized to almond-sized, well defined, superficial plaques; (2) less clearly outlined, pea-sized to walnut-sized, raised, erythematous nodules with violaceous halos, some arcuate and some with corymbose configuration, protruding above the skin, adherent to it and with the greater mass infiltrating the subcutaneous tissues, and (3) more or less diffused, similarly sized masses that are entirely submerged under the skin and found only on deep palpation; they are easily compressible on moderate diascopic pressure, leaving a yellowish to a brownish color. There are large lymph nodes in the cervical, epitrochlear and inguinal regions, reaching the size of a walnut in the last-named area.

The results of routine laboratory tests, including a chemical examination of the urine for phosphates, were normal. The lipid partition of the blood showed

435 mg. of total lipids (normal 500 to 700 mg.) per hundred cubic centimeters. General medical, ophthalmoscopic and rectal examinations, fluoroscopic and electrocardiographic examination of the heart and roentgen ray examinations of the long bones and chest revealed no abnormalities except osteochondrosis of the right tibia. There were no lesions in the nose, throat or larynx.

A histologic section taken from one of the cutaneous nodular lesions and examined by Dr. Sachs was diagnosed as sarcoid (Boeck type) with the following description: "Extending throughout the entire cutis and also in the fat area were a number of focal collections of epithelioid cells. Some of these were isolated and some fused. There was little cellular reaction about these tubercles. Some of the vesicles in the subepidemic region were considerably dilated. The overlying epidermis showed no important change. Rete pegs and papillary bodies were retained."

The right inguinal gland was removed and examined by Dr. Arthur C. Allen. The gross examination showed that the specimen was half of an oval nodule, 2.5 by 1.5 by 1.5 cm., well encapsulated and showing on section a light tan, translucent, homogeneous surface. Microscopic sections revealed that practically the entire lymph node was replaced by a form of tubercle composed of a loose scattering of histiocytes or epithelioid cells and lymphocytes, which were enmeshed in dense, concentric or interlacing bands of hyalinized collagen. With the azure blue stain the collagen was colored various shades of pink. No caseation or giant cells were seen. Between the tubercles were bands of lymphocytes, reticulum cells and plasma cells, a residuum of the original parenchyma of the node. The capsule of the node was slightly thickened. No acid-fast organism could be demonstrated by special stain. The diagnosis was Boeck's sarcoid of the lymph node with extensive fibrosis.

A section of the left inguinal gland was excised and injected subcutaneously into two guinea pigs and intraperitoneally into two more guinea pigs. The reactions to tuberculin tests of the guinea pigs were negative after four weeks. One animal is sick. The patient showed gradually increased sensitivity to tuberculin. On September 10 he gave a 1 plus reaction to a 1:5,000 dilution of old tuberculin. On September 18 he showed a 3 plus reaction to the same concentration.

The patient was treated with diphtheria toxoid on October 11, six weeks after the last tuberculin test. His lesions have undergone progressive resolution since then, a change in the appearance, size and consistency being already noticeable on the following day. He had no fever or any other untoward symptoms. The greatest response was in the subcutaneous and the deeply situated lesions, especially noted in the growth in the epigastric region, which was the size of a walnut and which had regressed by October 21, ten days after the injection, to the size of a pea. The left inguinal, cervical and epitrochlear lymph nodes have become smaller. All the lesions are softer, flatter and appreciably diminished in size. Another injection of 0.5 cc. of alum-precipitated diphtheria toxoid was injected subcutaneously on October 24.

The sedimentation rate (Westergren method) on November 1 was 4 mm. in one hour (normal, 18 mm.). The patient had already had by this time four injections of alum-precipitated diphtheria toxoid subcutaneously in the left arm, the first dose being 1 cc. and the three subsequent doses 0.5 cc. each. There was a general flattening of all the lesions with a diminution in size especially in the subcutaneous masses. The cervical and inguinal lymph nodes were barely palpable. He stated that he had a headache for the first time in three weeks on November 18, which lasted one-half day and was fairly mild. Rather severe headaches used to occur about once or twice a week and last one and one-half days.

DISCUSSION

DR. FRANK C. COMBES: I should like to hear Dr. Wise's explanation as to why the diphtheria toxoid has affected this eruption.

DR. EDWARD R. MALONEY: I think it will be confusing to label the condition in this case generalized sarcoidosis. I agree with the diagnosis of sarcoid

for the individual lesions, but the term generalized sarcoidosis is usually applied to sarcoidosis with lesions of the bones, larynx and viscera. In this case there are none of these lesions, and I think it would therefore be better to call the condition generalized cutaneous sarcoidosis. The internist encounters a great many cases of generalized sarcoidosis, and he has come to understand pretty well that they consist of lesions of sarcoid in the larynx, the bones and the viscera. If the condition in this case, in which the lesions are limited to the skin and subcutaneous tissues, is called generalized sarcoidosis, I am afraid the picture will be confused. I thought the glands which were involved were superficial and subcutaneous.

DR. FRANK C. COMBES: In regard to what Dr. Maloney said, why not refer to this condition as Schaumann's disease or benign lymphogranulomatosis? In this condition there may be involvement of the skin, lymph nodes, tonsils and bone. The patient's tonsils have been removed. The skin and lymph nodes are involved, although the bones are not; they may be involved at some later time.

DR. EDWARD R. MALONEY: In most of the cases of generalized sarcoidosis the cutaneous lesions are very few or nonexistent, the lesions being in the bones and internal organs.

DR. J. GARDNER HOPKINS: It was stated that the histologic picture is typical of Boeck's sarcoid, and a lesion was described running down into the subcutaneous fat. There were other lesions which clinically seemed to be all in the subcutaneous tissue. This seemed to me to be more typical of the Darier-Roussy type of sarcoid.

Pityriasis Rubra Pilaris. Presented by DR. EUGENE F. TRAUB.

A. V., a man aged 46, presented himself at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital about four weeks ago. He stated that an eruption appeared about two months previously. This was most prominent on the face, scalp, upper extremities and the upper part of the trunk but gradually spread to become generalized, involving the palms and soles with considerable thickening. The eruption began as tiny follicular papules which coalesced to form patches, and as these patches coalesced, particularly on the upper part of the trunk, islands of normal skin were left which contrasted strongly with the involved areas with their erythema and scaling. The typical horny spicules about the hair follicles on the dorsal surfaces of the fingers were not present, at least not in an appreciable degree. The eruption was rapid in its development and spread.

The Wassermann reaction was negative. The urine was normal. The report on vitamin studies was as follows: Vitamin A, 70 U. S. P. units (normal, 65 to 100 U. S. P. units) and carotene, 58 mg. (normal) per hundred centimeters of blood.

The patient has been receiving 200,000 U. S. P. units of vitamin A daily, with what appeared to be decided initial improvement; however, further improvement did not follow through, but rather the process continued to spread.

Three sections were removed for microscopic examination and were reported on as follows: 1. Microscopic diagnosis: hyperkeratotic lesion with microscopic bullae high in the epidermis. The section showed a moderately acanthotic epidermis with a swelling of the prickle cells in places in the upper layers. There was a thick scale that was occasionally parakeratotic, and when the scale was thickest the granular layer was absent. Occasionally there was what appeared to be serum and cellular detritus between the epidermis and the scale, which gave the appearance of a superficial bulla. There were slight edema and some cellular exudate in the upper part of the corium. 2. Microscopic diagnosis: indeterminate. The section showed an epidermis with some fusion of rete pegs. A thin granular layer with a number of perinuclear spaces was seen in the upper part of the prickle cell layer. A lamellated scale that was largely nonparakeratotic was observed. The changes in the corium were slight. In one area there was some serum between the epidermis and overlying scale, as though it might be the edge

of a perifollicular area. 3. Microscopic diagnosis: dermatitis, possibly pityriasis rubra pilaris. The section showed a fairly normal epidermis with a parakeratotic scale near the follicle openings. The lymph spaces and some of the blood vessels were dilated. There was a large amount of intercellular edema as well as intracellular edema of the collagen fibers.

DISCUSSION

DR. HOWARD FOX: I agree with the diagnosis in this classic case. The anterior part of the trunk shows the typical acuminate papules in the neighborhood of the solid diffuse areas. There is one peculiar feature of this disease, on which I made a tentative diagnosis from a distance. This consists of small round areas of normal skin which appear to be sunken slightly in the diffuse red areas. I have never heard this discussed, but I have often noticed it.

DR. PAUL E. BECHET: I agree with the diagnosis. As Dr. Fox has stated, the lesions are typical of that disease.

DR. FRANK C. COMBES: I agree with the diagnosis in spite of the histologic report, which seems to be uncertain.

DR. FRED WISE: I think that clinically this is a classic case.

DR. EUGENE F. TRAUB: I should appreciate suggestions for therapy, especially in reference to vitamins.

DR. GEORGE C. ANDREWS: I suggest treatment with liver extract.

DR. EDWARD R. MALONEY: I agree with the diagnosis as presented.

DR. J. GARDNER HOPKINS: I believe the response to vitamin therapy in cases of this kind has been varied. Brusting reported a favorable result. Gross had a case in which there was benefit from the use of liver or nicotinic acid.

DR. HOWARD FOX: As a medical student I saw my father's patient whose picture appears in his atlas (Fox, G. H.: Photographic Atlas of the Diseases of the Skin, Philadelphia, J. B. Lippincott Company, 1900-1905). After having tried all known methods of treatment, he finally induced her to live at the seashore, where she remained in perfect health for thirteen years. That of course was before the days of vitamin therapy.

DR. EUGENE F. TRAUB: What struck me in this case in the beginning was the point which Dr. Fox mentioned, namely, the areas of normal skin occurring on the chest and trunk in the midst of all the surrounding erythema and keratotic follicular lesions. I pointed this out as occurring chiefly in this condition, and I am glad to hear Dr. Fox say he has never seen it in any other condition.

DR. GEORGE C. ANDREWS: Mycosis fungoides will show the same thing.

DR. A. BENSON CANNON: An exfoliating type of dermatitis from tuberculosis will cause white spots such as are seen in this patient.

Dermatitis Herpetiformis. Arsenical Pigmentation and Keratosis. Presented by DR. PAUL E. BECHET.

J. B., a man aged 32, from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, states that his eruption has been present without intermission for six years. On inspection, symmetric, grouped, greatly reddened, vesiculobullous patches are observed on the trunk, thighs and buttocks. The patches are excoriated, crusted and torn from excessive scratching, the result of an intense pruritus greatly interfering with the patient's rest. The trunk presents a diffused grayish pigmentation. On palpation the skin feels dry and harsh. The palms exhibit a severe degree of hyperkeratosis, with numerous verrucosities. The patient states that he has taken from 1 to 30 drops of solution of potassium arsenite U. S. P. daily for three years.

DISCUSSION

DR. EUGENE F. TRAUB: I agree with both diagnoses. I think the case is a classic one.

DR. HOWARD FOX: I should like to know what the experience of the members of this society is regarding the outcome of such keratoses. I understand, of course, that some of them become cancerous. Do the others last indefinitely, or do any of them disappear spontaneously?

DR. GEORGE C. ANDREWS: In the cases I have observed these lesions have lasted indefinitely. The patients pick out the little black spots, and then there is a little depression; but the plug gradually returns after a few months. Ultimately some of the lesions become cancerous, as has been said.

DR. R. H. RULISON: As far as I know, these warty lesions last indefinitely.

DR. FRANK C. COMBES: I agree with the diagnosis. As has been said, some of these lesions become cancerous. I wonder how many cases have been observed in which keratoses of the palms became cancerous.

DR. J. FRANK FRASER: I observed a case of generalized pigmentation accompanied by keratoses of the palm in which multiple squamous cell epitheliomas developed. The lesions developed two to three years after the administration of arsenic had been discontinued (I do not recall the exact number). When these lesions become malignant, the epitheliomas are always of the squamous cell type. I have never seen the basal cell type develop in arsenical keratosis.

DR. A. BENSON CANNON: Usually arsenical keratoses begin to appear two to three years after the patient has begun arsenic treatment and usually increase in number and size for the next eight to ten years. I should think it would be worth while to try to eliminate the arsenic from this patient in order to prevent an aggravation of the keratoses.

DR. FRANK C. COMBES: How would you get rid of the arsenic in a patient?

DR. A. BENSON CANNON: I believe arsenic can be eliminated in cases of arsenical retention by means of sweating, forced fluids, suitable diets and sodium phosphate by mouth and by injection of calcium thiosulfate. Arsenic is a cumulative drug, and the symptoms of keratoses and café au lait spots are not likely to appear until some years after its use. I think that because of the widespread pigmentation and keratoses in this patient and the fact that they appeared so soon after he commenced taking arsenic, one might expect a progressive increase in the lesions in the event that the metal has not been eliminated.

DR. PAUL E. BECHET: I have a private patient under observation now who will partially answer Dr. Fox's question. He is a man of 65 who took solution of potassium arsenite U. S. P. as a child for chorea for several years. He has had arsenical keratoses of the palms and fingers for fifty years, and I have been observing him for the past eight years. These keratotic patches become aggravated, but none of them has become malignant. However, he has had dozens of epitheliomas of the superficial type on the sites of old arsenical keratotic patches on the body which readily yielded to mild destructive methods. He showed an abnormally increased content of arsenic in the urine. After the patient was given sodium thiosulfate orally and intravenously for a year, the arsenic disappeared completely from the urine, and his skin was definitely softer and the keratoses lessened. He discontinued taking the drug for about a year, and the condition recurred, accompanied by an excessive amount of arsenic in the urine, which a second course of sodium thiosulfate eliminated with substantial improvement in the condition of the skin.

DR. GEORGE C. ANDREWS: In this connection I should like to say that I have had 2 patients with arsenical keratoses who have been benefited by the oral administration of sodium thiosulfate, for they have not had any more keratoses. They have taken it for five years or more.

DR. PAUL E. BECHET: I agree that something should be done for this man. He has ten or twelve verrucous growths on the palms now. The disease is extensive. I still believe in the benefits of sodium thiosulfate sufficiently to recommend its use in this case.

Granuloma Annulare. Presented by Dr. J. Frank Fraser.

I. R. V., a physician aged 32, was presented before this society on Oct. 28, 1941 (Arch. Dermat. & Syph. **45**:811 [April] 1942). Under roentgen ray treatment the lesion has disappeared.

BRONX DERMATOLOGICAL SOCIETY

Van Alstyne H. Cornell, M.D., *President*

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Nov. 27, 1941

A Case for Diagnosis (Chrysiasis?). Presented by Dr. Adolph Rostenberg.

A patient aged 35, a housewife, was taken ill about two years ago with a severe attack of polyarthritis, for which she received a variety of internal medication. In April 1941 her physician instituted a course of intramuscular injections of gold sodium thiosulfate, giving her a total of fourteen injections at weekly intervals. After the sixth injection her eyelids became swollen and itchy. At the same time she began to complain about irregular uterine bleeding. Following the eighth injection an eruption appeared on the buttocks and legs accompanied by severe itching. The treatment was continued until a generalized desquamating dermatitis developed.

When first seen on August 5, the patient presented a severe generalized exfoliative dermatitis. After eight intravenous injections of calcium thiosulfate and local medication the eruption began to clear and the skin began to assume a normal appearance. At that time, however, a diffuse pigmentation was noticed.

The discoloration involves the buttocks, back and legs and is seen in small areas under both eyelids and on the forehead, cheeks and lips. There is a sharply defined patch in the V of the neck. The color of the pigmented areas is slate gray with a faint bluish tinge. There are no subjective symptoms.

DISCUSSION

Dr. Samuel M. Peck: I do not believe that this case is one of pigmentation due to gold. In chrysiasis the color is purplish red and the pigmentation is not in patches but generalized. This condition suggests the end stage of an inflammatory process. The impregnation of melanin is due to its deposit in the cutis during the period when the epidermis showed considerable edema.

Dr. David Bloom: I believe that the pigmentation present is due not to deposition of gold but rather to melanin following a dermatitis from gold medication.

Dr. Arthur Sayer: The presenter could give more valuable evidence in substantiation of the diagnosis of chrysiasis by a spectroscopic analysis of the affected skin. A histologic study of the tissue will show the presence of metallic granules in the upper part of the cutis, but it is not possible to identify the specific nature of these granules except by special staining chemical reactions.

Dr. Henry Silver: The diagnosis of chrysiasis could be easily established even without histologic examination if the total amount of gold administered were known. It has been shown that chrysiasis develops if the total dose reaches 150 mg. of gold sodium thiosulfate per kilogram of body weight. On the other hand, if the total amount is less than 50 mg., chrysiasis is less likely to occur. It would be interesting to hear from Dr. Spiegel about his experience with the spectrographic method.

Dr. Leo Spiegel: I believe this patient has a pigmentation of the skin which represents the end result of an exfoliative dermatitis caused by the injections of

a gold compound. It is not a discoloration due to deposition because the pigmentation is distributed unevenly in blotchy patches of irregular size and outline. The injections of gold were given intramuscularly, and if this condition were chrysiasis of the skin the deposit of the heavy metal would be at the site of the injections. Unfortunately, biopsy was not permitted. By the spectrographic method the gold line of the spectrum could be readily determined. Also, by dark field examination the foreign particles could be readily detected in the upper layers of the corium.

DR. CHARLES R. REIN: This patient states that the pigmentation has faded considerably during the past two months. This fact speaks against a diagnosis of chrysiasis and in favor of that of pigmentation following a long-standing and severe dermatitis.

DR. FREDERICK REISS (by invitation), Shanghai, China: There is a peculiar feature in this case which has not been pointed out, namely, the reticular distribution of the pigmentation in the iliosacral region. This almost resembles livedo calorica.

DR. ADOLPH ROSTENBERG: I admit that the diagnosis of chrysiasis is rather hazardous without a biopsy. My diagnosis is based on clinical grounds alone. The color is bluish and is not that of the pigmentation following a severe dermatitis. I could not ascertain the exact quantity of gold administered, but I judge that the amount was large.

Arsenical Keratoses and Squamous Cell Epitheliomas in a Psoriatic Patient. Presented by DR. SAMUEL M. PECK.

F. S. C., a man aged 45, a butcher, has suffered from psoriasis since the age of 14. His mother was also afflicted with psoriasis. For the past three and one-half years he has received arsenic in the form of drops, with resulting improvement. Recently two painful lesions appeared on the left palm between the thenar and hypothenar regions. The lesions were treated by electrocoagulation by his physician but failed to heal.

When he was first seen, on July 30, 1941, there were two hyperkeratotic and slightly necrotic painful infiltrations, measuring on the surface 1.5 by 1.7 cm. A clinical diagnosis of squamous cell epithelioma was made.

The histologic examination by Drs. Satenstein and Sachs showed the epidermis to be extremely acanthotic and verrucous. Under the epidermis there was a substantial small round and plasma cell infiltration. Within the epidermis there was considerable anaplasia with some whorl and pearl formation. The basal cell margin appeared to be intact. There was considerable keratinization on the surface. At one point there was a large abscess within the epidermis. The histologic diagnosis was prickle cell epithelioma.

From August 6 to August 29 a total of 4,000 r of unfiltered roentgen rays was given. At the end of September these areas appeared clinically cured.

At present the patient shows psoriatic patches on the trunk and soles. There are multiple verrucous lesions on the fingers and on the palms; some are annular, and others show black pigmentation. There is one lesion measuring about 0.75 cm. in diameter at the base of the end phalanx of the left fifth finger.

Arsenical Keratoses. Presented by DR. LOUIS CHARGIN.

P. K., aged 51, a laborer, had suffered from psoriasis for many years. The disease has varied in extent but is now controlled. The patient states that for two years, from 1916 to 1918, he regularly took drops by mouth which he definitely identifies as having been arsenic. The drops were evidently given by his physician for the psoriasis. For the past fifteen years lesions have been developing on the palms and soles which have persisted to date.

There are many scattered small flat keratotic lesions on the palms and soles. These are dry, painless and not fissured and show no tendency toward ulceration. They resemble warts or the lesions observed on the palms in Darier's disease.

DISCUSSION OF CASES OF ARSENICAL KERATOSES

DR. SAMUEL M. PECK: Most textbooks erroneously state that pentavalent arsenic is responsible for malignant conditions due to arsenic. It is agreed that in the majority of cases it is solution of potassium arsenite U. S. P. that is at fault. The formula for arsenic trioxide is AS_2O_3, and, unless I am mistaken, this solution contains a trivalent arsenic. I agree that it is the inorganic rather than the organic arsenic which is usually at fault. Stokes stated that he has never observed epithelioma following the use of arsphenamine. I heartily agree with him, and I think that there is too much fear about the use of arsphenamine in the treatment of leukoplakia.

DR. GIRSCH D. ASTRACHAN: At the New York Post-Graduate Medical School and Hospital Drs. MacKee, Rosen and Satenstein have expressed the opinion that arsenotherapy may activate buccal epithelioma.

DR. LEO SPIEGEL: I have never seen epitheliomas as described by Dr. Peck, nor have I observed keratoses following the use of arsphenamine or pentavalent arsenicals, such as tryparsamide or aldarsone (sodium methylenesulfonaminohydroxyphenylarsenate). However, in many cases I have seen epitheliomas following the use of solution of potassium arsenite U. S. P.

DR. FRANK E. CROSS: In patients with gumma of the tongue arsenic will hasten the development of cancer.

DR. DAVID BLOOM: Several years ago I had occasion to review a monograph by a Dutch author on the effect of arsenic on psoriasis. Basing his conclusion on investigation of many cases of psoriasis, the author stated that arsenic is as a rule ineffective in psoriasis.

DR. MARK KROLL (by invitation): It must be remembered that in many cases leukoplakia on a syphilitic basis tends to become malignant without arsenical therapy.

Basal Cell Epithelioma in Lupus Erythematosus. Presented by DR. SAMUEL FELDMAN.

P. A., aged 75, formerly a newspaperman, states that he has had an eruption for about thirty years. Following a severe sunburn red patches remained on the face, back and hands. The patient was treated with ointments and had some of the patches "burned out with electricity." The patches healed leaving white areas. Several months ago "sores" developed on the left side of the nose and near the ear. Soon an ulceration appeared on the back, on the site of a lesion which had been present for ten years.

There are a number of erythematous patches on the face. Some of these are partially atrophic, and others are covered with adherent scales. Spicules are occasionally seen on the under surface of the scales when they are removed. Dilated follicles are not much in evidence. On the nose there is a considerable amount of telangiectasia. On the left side of the nose there is an ulceration showing thick, rolled and pearly edges. A smaller and less infiltrated ulceration is present in front of the ear. On the back there is a red scaly flat lesion about 1 inch (2.5 cm.) in diameter. There are several slight elevations on the surface of that lesion. Near the upper margin there was originally an ulceration which was diagnosed clinically as basal cell epithelioma. The ulcerated portion was removed for histologic study. The histologic diagnosis was basal cell epithelioma.

Histologic examination of a specimen removed from an area which showed only erythema and scaling showed the hair follicles moderately dilated and filled with horny plugs. In the papillary layer the collagenous bundles were normal and the elastic tissue was practically absent. There was a sparse cellular infiltration below the papillary zone, somewhat less in amount than is usually seen. The collagenous material in the middle layer of the cutis was homogeneous and became bluish when stained with hematoxylin and eosin and almost black with

Weigert's elastic tissue stain. The elastic tissue was clumpy and broken up into coarse and fine granules. The epidermis was for the most part normal. In one small well circumscribed area the cells lost the prickles and were separated from one another by clear spaces of considerable size. The shape of the cells was altered. Some cells were oblong and some triangular or pear shaped. The nuclei were large, deeply stained and surrounded by a comparatively small amount of protoplasm. In this area, the various layers of the skin were hardly distinguishable from one another. The diagnosis was lupus erythematosus with the early stages of Bowen's disease.

DISCUSSION

DR. CHARLES A. GREENHOUSE: My tentative diagnosis of this unusual condition is multiple basal cell epithelioma. I do not find any evidence of lupus erythematosus. It is uncommon to see multiple epitheliomas in the lesions of lupus erythematosus. Moreover, according to most observers, the type of epithelioma that arises from lupus erythematosus is more likely to be of the prickle cell type.

DR. HENRY SILVER: It is surprising to find basal cell epithelioma in lupus erythematosus. Epithelioma on the basis of lupus erythematosus is not as uncommon as is usually believed. It occurs more frequently in men than in women, particularly in patients treated locally with acids or roentgen rays. The type, as a rule, is prickle cell epithelioma.

DR. FRANK E. CROSS: I am in agreement with Dr. Greenhouse's diagnosis of multiple basal cell epithelioma.

DR. SAMUEL FELDMAN: The resemblance of the lesions to superficial basal cell epithelioma is the reason for presenting the patient. The erythematous eruption completely covers the face. The presence of numerous white and atrophic areas distorted the original picture. The tip of the nose is atrophic, and there is a certain amount of absorption of cartilage. The ulcer on the nose is surrounded by an area of telangiectasia. These findings would seem to indicate the presence of lupus erythematosus. The lesion on the hand is red and scaly with a clear and somewhat atrophic center, which is characteristic of lupus erythematosus.

Urticaria Pigmentosa in a Syphilitic Adult. Presented by DR. HENRY SILVER.

H. I., a white man aged 38, a patient of Dr. H. Victor Mendelsohn, was first seen on Jan. 24, 1938, because of a patch of alopecia and latent syphilis. He had received elsewhere twenty intravenous injections and forty intramuscular injections. Some of the injections in the arm caused minor gastrointestinal upsets. The patient presented no evidence of syphilis or other lesions on any part of the mucocutaneous surface except a patch of alopecia the size of a 25 cent piece on the lower part of the right occipital area. The Wassermann reaction was 4 plus, and on examination the spinal fluid was normal.

He was given further antisyphilitic treatment, and on May 16, 1938, when he had received fourteen injections of neoarsphenamine and an equal number of injections of a bismuth preparation, a group of erythematous and slightly pruritic papules the size of a lentil appeared on the left side of the abdomen. They soon flattened and assumed the present size, shape and color. Additional treatment with the aforementioned drugs and the ingestion of cathartics containing phenolphthalein did not aggravate the eruption. Since the onset, new crops of lesions have appeared on different parts of the cutaneous surface, until the eruption is fairly generalized. The newest lesions appeared about four weeks ago. None of the lesions has disappeared completely.

Sparsely distributed over the neck, trunk, upper and lower extremities and both soles are ovoid and circular macules varying in size from that of a pinhead to that of a split pea. The hands, palms, face and scalp do not share in the eruption. The mucosae are normal. On rubbing, slight elevation of the lesions

occurs, with redness of the surrounding skin. The lesions are always free of scaling and cause no subjective symptoms except slight pruritus for a few minutes when they first appear.

On the right side of the neck, slightly above the hair line, there is a patch of alopecia the size of a nickel which has recurred for the fourth time in the same area.

Histologic examination of one of the typical lesions showed urticaria pigmentosa. The sections were stained with hematoxylin and eosin, thionine and McNeal's tetrachrome stain for mast cells.

DISCUSSION

DR. FRANK E. CROSS: I am inclined to think that urticaria pigmentosa bears no relation to the administered arsphenamine but is merely a coincidence.

DR. DAVID BLOOM: One point is of particular interest to me, namely, the appearance of the eruption in the course of antisyphilitic therapy. It is my impression that there is some causal connection between the two. I have seen lupus miliaris disseminatus appear in a white woman while she was receiving antisyphilitic therapy. In 1 of the cases of tuberculosis cutis reported by Dr. Mendelsohn and me, that of a Negress, this condition also developed in the course of antisyphilitic therapy (ARCH. DERMAT. & SYPH. **36**:937 [Nov.] 1937). I am not able to state what the exact connection is.

DR. CHARLES LERNER: From a theoretic standpoint it is worth remembering that syphilis stimulates the reticuloendothelial system and also produces pigmentary disturbances. Although I do not believe that the syphilitic process itself can produce urticaria pigmentosa, I am inclined to think that, so far as the reticuloendothelial system is concerned, there may be a connecting link in the pathogenesis of this disease.

DR. LOUIS CHARGIN: I have never encountered a case of urticaria pigmentosa as a result of antisyphilitic therapy. If arsphenamine therapy is further indicated in this case it may be given with safety.

DR. SAMUEL M. PECK: The color of urticaria pigmentosa is partly due to the melanin in the epidermis, which is not considered in the class of nevi. The French school of dermatology introduced the conception of biotropism to explain the scarlatiniform and measles-like eruptions seen after ingestion of drugs. According to this conception a latent virus infection was actually responsible for the cutaneous manifestations. The virus was made active by some sort of mechanism invoked by the drug. I do not believe that this concept has ever been proved.

DR. PAUL GROSS: I believe in biotropism, and I am willing to apply the theory to nine day erythema, tuberculosis and even lichen planus, with which the possibility of a virus infection still exists. As little as is known about urticaria pigmentosa, infection certainly is the least probable cause, and therefore the discussion of biotropism is not applicable to this disease.

DR. GIRSCH D. ASTRACHAN: I have observed many cases of ordinary urticaria following injections of arsenicals or bismuth, but I have never encountered a case of urticaria pigmentosa following these injections. I think the presence of urticaria pigmentosa in this case following the use of arsenicals is merely coincidental.

DR. ERNST W. NATHAN (by invitation): The relation of arsphenamine therapy and cutaneous eruptions has been discussed by Buschke and others. One has to distinguish between two different types of possible reactions: (1) toxic or allergic reactions of the skin and (2) latent diseases of the skin which are not actually toxic manifestations caused by the arsphenamine itself. As an example, lichen-planus-like eruptions appearing during arsphenamine treatment may be cited. Analogous to these observations one could assume that an urticaria-pigmentosa-like syndrome could have been provoked as a reaction of the skin to arsphenamine.

DR. H. VICTOR MENDELSOHN (by invitation): I do not think that the antisyphilitic treatment was responsible for the appearance of the eruption. I believe

this condition is acquired urticaria pigmentosa in a syphilitic person and would have appeared irrespective of treatment. The only point of interest that the antisyphilitic treatment may have in this case is its failure to cause the eruption to disappear. Dr. Fred Wise, in discussing a case of urticaria pigmentosa presented by Dr. J. J. Eller (ARCH. DERMAT. & SYPH. **39**:751 [April] 1939), mentioned a report in the literature of an alleged cure obtained in 4 cases of this disease with injections of a bismuth preparation. The results of bismuth therapy in this case would not support this view.

The color of the lesions is believed by some to be due to an increased amount of the ordinary pigment of the epidermis; others believe that it depends on the mast cells as well as the amount of pigment.

DR. HENRY SILVER: It is important to establish this case as one of urticaria pigmentosa because of the discussion centered around the occurrence of the disease in a syphilitic patient. The diagnosis of urticaria pigmentosa rests on two characteristics, aside from the morphologic picture: One is clinical, the well known urticaria factitia; the other is histologic, the presence of the mast cells. That the diagnosis in the adult may clinically present difficulties is known. This patient presents the characteristic features of urticaria pigmentosa mentioned. Dr. Chargin stated that he has never seen urticaria pigmentosa following antisyphilitic treatment. Moreover, one seldom finds a recorded case of urticaria pigmentosa associated with syphilis.

A Case for Diagnosis (Sycosiform Eruption of the Face in a Woman). Presented by DR. SAMUEL M. PECK.

H. L., a woman aged 32, was previously presented at the November 1941 meeting of the Section of Dermatology and Syphilis of the New York Academy of Medicine.

The patient is represented because of the considerable improvement following the use of chlorhydroxyquinoline (quinolor) ointment.

Histologic examination of a lesion of the upper lip showed intrafollicular and perifollicular chronic inflammatory reaction.

DISCUSSION

DR. DAVID BLOOM: I have seen the patient elsewhere, and the first impression was that of keratosis follicularis (Darier). However, because of the association of the cutaneous lesions on the oral mucosa and on the palpebral conjunctivas I now consider the condition lupus erythematosus.

DR. CHARLES WOLF: Various diagnoses were considered in this case. It is known that lupus erythematosus is an ephemeral disease. It changes spontaneously, and the lesions tend to improve. This improvement is only transitory. The lesions of the mucous membrane strongly suggest lupus erythematosus.

DR. CHARLES LERNER: I think that sycosis vulgaris should be strongly considered in this woman. I have never seen sycosis vulgaris on the face of a woman, but I do not see why it cannot occur. I noticed the limitation of the lesions to the upper lip and regions of the eyebrow; each definite pustular follicular lesion was pierced through the center by a hair. The color of the lesions was also strongly suggestive of sycosis vulgaris. The fact that Dr. Peck has obtained improvement with the ointment tends to corroborate that diagnosis. I am inclined to think that the condition of the soft palate is independent of the cutaneous disease from which this patient is suffering.

DR. LOUIS CHARGIN: This process began about six months ago, and it was not until much later that lesions of the mucous membrane appeared. Because of these lesions tuberculosis was suspected, but histologic study failed to confirm this. I am against the diagnosis of lupus erythematosus because an eruption of this type persisting for so long should show some evidence of atrophy.

DR. SAMUEL FELDMAN: Sycosis vulgaris may be seen in women but not on the face. It is usually called folliculitis.

DR. PAUL GROSS: Lesions on the lip would not necessarily speak against the diagnosis of sycosis. The possibility of acrodermatitis continua Hallopeau with lesions of the mucous membrane should be considered.

DR. DAVID BLOOM: There is a superficial type of lupus erythematosus which may persist for years without leaving scars or atrophy.

DR. SAMUEL M. PECK: I do not believe that the diagnosis is either lupus vulgaris or lupus erythematosus. Frankly, I do not know just where to classify this condition.

Pityriasis Rosea with Palmar, Plantar and Genital Lesions. Presented by DR. WILLIAM LEIFER.

F. R., a white man aged 47, was previously presented before the Section of Dermatology and Syphilis of the New York Academy of Medicine on Nov. 5, 1941 (ARCH. DERMAT. & SYPH. **45**:832 [April] 1942). He is presented again to show the spontaneous change in the appearance of the eruption in the three weeks which has elapsed.

DISCUSSION

DR. WILLIAM LEIFER: My diagnosis when the case was first presented was the same as the one given tonight. Previously three diagnoses were considered: pityriasis rosea, pityriasis lichenoides et varioliformis acuta and lichen planus.

DR. CHARLES A. GREENHOUSE: My tentative diagnosis is pityriasis lichenoides et varioliformis, the diagnosis made by Dr. Chargin when this case was first presented. One sees tonight a polymorphous eruption, composed of lesions resembling those of pityriasis rosea, lichen planus, parapsoriasis and also crusted umbilicated varicelliform-like papules.

DR. FRANK E. CROSS: Pityriasis rosea has a rather definite distribution, which is lacking in this case. I previously suspected that in a week or two lesions of lichen planus would develop. However, parapsoriasis seems to be the likely diagnosis now.

DR. PAUL GROSS: It is important in cases of extensive pityriasis rosea to remember that acute lichen planus may greatly resemble pityriasis rosea. If one has observed the gradual transformation into lichen planus, one realizes the difficulty of an early diagnosis in the acute stage.

DR. CHARLES WOLF: When the patient was previously presented I stated that the eruption was lichen planus and that a biopsy should be performed to corroborate this diagnosis. Tonight a biopsy is no longer necessary, as the condition is lichen planus without question.

DR. WILLIAM LEIFER: In answer to Dr. Gross, I should like to mention Dr. Fred Wise's comment on this case. He stated that if he looked only at the eruption on the trunk, he would make a diagnosis of pityriasis rosea.

A Case for Diagnosis (Acrodermatitis Hiemalis?). Presented by DR. DAVID BLOOM.

E. W., a woman aged 56, came to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Oct. 10, 1941 presenting an eruption on the legs which had recurred every winter for the past ten years. The family and past histories were essentially irrelevant.

On the outer side of the right leg there are about half a dozen round brown plaques varying in size from that of an oval pea to that of a quarter of a dollar, some of which show atrophy. On the inner aspect of the lower portion of the left leg there are a few hemorrhagic lesions, about 2 cm. in circumference, some of which show superficial necrosis.

During the last few weeks there was an opportunity to observe the evolution of these lesions. Following a spell of cold weather purpuric lesions appeared on the legs; they gradually changed to blackish hemorrhagic lesions and resulted in superficial necrosis of the skin. Thus various types of lesions were seen simultaneously: purpuric spots, hemorrhagic and necrotic lesions and ulcerative lesions.

The Wassermann reaction was negative. Examination of the urine showed no abnormalities. The total erythrocyte and leukocyte counts and the differential count were normal except for 5 per cent eosinophils.

The histologic examination showed a flattened epidermis with consequent disappearance of the rete pegs. The superficial blood vessels were dilated. There was some hemorrhage in the perivascular infiltration.

DISCUSSION

DR. ARTHUR SAYER: It would be additional proof that the eruption is due to sensitivity to cold if similar or urticarial lesions would develop after exposure to cold water. In some patients this type of reaction develops after bathing in cold water even in the summer months. The cold air (or cold water) produces a reaction in the blood vessels of the upper part of the cutis with resulting hemorrhagic bullae and petechiae.

DR. MAX BERKOVSKY: This patient should be given a trial of histaminase. The use of this remedy in the treatment of cold allergy has resulted in improvement.

DR. FREDERICK REISS (by invitation), Shanghai, China: I wonder whether cold allergy should be considered as hyperergy. As far as I know, passive transfer has never been successful. Therefore, it seems doubtful whether histaminase would be successful. It could be tried at any rate. I experimented with histaminase and in 1 case of pruritus produced urticaria.

DR. SAMUEL M. PECK: A definite diagnosis cannot be made in a case such as this without a thorough hematologic and capillary study. It strikes me that cold alone would not explain the clinical picture in this case.

DR. ERNST W. NATHAN (by invitation): I agree with Dr. Peck. The case should be studied from the endocrinologic standpoint, since conditions of this type have been observed in combination with hyperthyroidism or with other disturbances of the thyroid gland. They have also occasionally been observed in combination with functional disorders of the ovaries. Sometimes disturbances of the capillary function can be demonstrated by microscopic examination of the capillaries (capillary microscopy).

DR. DAVID BLOOM: The patient has had studies made in the department of hematology, including tests for cold allergy, and was found normal in every respect. This condition undoubtedly is a vascular disturbance, and a study of the vascular system is indicated.

NEW YORK ACADEMY OF MEDICINE, SECTION OF DERMATOLOGY AND SYPHILIS

LOUIS TULIPAN, M.D., *Chairman*

TIMOTHY J. RIORDAN, *Secretary*

Dec. 2, 1941

Pyoderma Gangraenosum. Presented by DR. MAURICE J. COSTELLO.

I. N., an unmarried Negress aged 23, is presented from Bellevue Hospital with an ulcer on the right leg. About ten years ago, following a bruise incurred against the edge of a table, a sore appeared, which soon became much larger.

After a year of local therapy with salves and powders, together with iron internally, the ulcer healed; but it recurred after about nine months and has never healed since.

The patient has received extensive antisyphilitic treatment for the past four years but pleads ignorance as to how she acquired the disease. Her past history is essentially irrelevant.

Examination shows a single oval ulcer, about 4 by 2 inches (10 by 5 cm.), located on the inner aspect of the lower third of the right leg. It has a clean, granulating base and is surrounded by thick, indurated, gray scar tissue.

The Wassermann and Kahn reactions were both 4 plus. The spinal fluid was essentially normal. The blood count was essentially normal. The urine was normal. A roentgen ray examination of the leg showed a localized osteoperiostitis involving the midshaft of the right tibia for about 1½ inches (4 cm.), with exuberant bone formation, probably syphilitic in origin.

Treatment has consisted of the local use of 5 per cent sulfathiazole (2-[para-aminobenzenesulfonamido]-thiazole).

DISCUSSION

DR. EUGENE F. TRAUB: The improvement in this patient's ulcer since I saw her at a meeting of the Metropolitan Dermatological Society two weeks ago is miraculous. I know of no method which could have produced an equal change, and I emphasize the point because I was somewhat skeptical of the value of sulfathiazole used locally. There is no question that in this case, at least, the local treatment has proved effective. The lesion was an open ulcer with raw granulations, and one can readily see just how much healing has taken place in two weeks.

DR. MAURICE J. COSTELLO: The reason sulfathiazole was not given by mouth is that I wanted to try it locally, thinking that it would be more effective because of the greater local concentration. I should have given it orally later if it had not been effective when applied in this manner. I have had such fine results from the local application of a 75 per cent sulfathiazole powder or a 5 per cent sulfathiazole cream in other instances that I thought it should be tried in this case.

Chronic Discoid Lichenoid Dermatitis Associated with Giant Follicular Lymphadenopathy. Presented by DR. FRANK C. COMBES.

S. Y., a white youth aged 18, was admitted to Bellevue Hospital complaining of an itching eruption on his trunk of three years' duration. The eruption first appeared in 1938, when he noticed a "spot" on his chest; soon similar lesions appeared on the trunk. The condition clears up in summer when the patient is exposed to the sun and reappears in the fall and winter. He has been hospitalized several times for this eruption.

There is a generalized papular eruption of lesions varying in size from that of a split pea to that of a dime on the trunk, on the inner aspects of the thighs, arms and forearms and on the face. Many areas of depigmentation are present and indicate the sites of previous lesions. There are many small discrete papules on the inner aspects of the thighs. Palpable glands are present in the axillas and inguinal regions.

Cytologic examination of the blood did not show any anemia, but on one occasion it showed 11 per cent eosinophils and on another occasion 16 per cent eosinophils. The Wassermann reaction of the blood was negative. Tests for fungi gave negative results. Examination of the urine showed no arsenic.

Microscopic examination of tissue taken from the skin showed a thin layer of keratin covering a hyperplastic layer of squamous epithelium. There was acanthosis with the interpapillary processes extending into the underlying cutis. In the

papillary layer there was a diffuse but moderate infiltration consisting of small round cells, a few plasma cells and an occasional eosinophil. One of the cervical lymph nodes showed changes characteristic of giant follicular lymphadenopathy.

The patient has had many forms of treatment, including roentgen irradiation and application of tar preparations. His condition improves while he is in the hospital but relapses when he is discharged unless the season is summer and he can derive the benefits of solar radiation. He has been treated with subcutaneous injections of sodium arsenate in gradually increasing doses. With this therapy the lesions have become flatter and the pruritus has lessened.

DISCUSSION

Dr. Paul Gross: The issue in this case ought to be made clear, namely, that chronic lichenoid and discoid dermatitis is not a precursor of a lymphoblastoma, even though a definite lymphadenopathy may be present. It should not be surprising, though, that a chronic persistent dermatosis with chronic inflammatory lymph gland involvement might in an individual case produce a lymphoblastoma.

Dr. Frank C. Combes: I had 2 cases of chronic discoid and lichenoid dermatitis in which sarcoma developed. This type of condition may end with sarcoma or Hodgkin's disease. Of my patients with giant follicular lymphadenopathy —about 15 of them—5 died of polymorphous cell sarcoma, and 1 of those had chronic lichenoid and discoid dermatitis.

Dr. Fred Wise: The eczematoid dermatitis to which Rosen was the first to call attention and which later was described in detail by Sulzberger and Pascher sometimes simulates mycosis fungoides and various manifestations of leukemia and pseudoleukemia. In this case the diagnosis of chronic recurrent discoid dermatitis may be readily accepted, even on cursory examination. With eruptions of this kind, the histologic examination shows no characteristic features, but it serves to eliminate various forms of leukoses. Though such eruptions are rebellious to treatment and are prone to erratic remissions and exacerbations, they eventually clear. They should not be confused with the disease described by Symmers as giant follicular adenopathy combined with polymorphous cell sarcoma of the lymphoid follicles.

Dr. Oscar L. Levin: I agree with Dr. Combes that the patient presents an erythroderma such as may be observed in leukemia. Giant follicular lymphoblastoma, described by Symmers and more recently by Baehr and Klemperer, shows cutaneous lesions resembling those seen in this patient. The pathologic changes in the lymph nodes are characteristic and may readily be differentiated from those in leukemia and Hodgkin's disease. This malady does not always have a rapidly fatal termination. Under proper treatment patients may live for many years. The glands may be localized to the neck or the enlargement may become generalized, and in the latter case the spleen is also involved. Death may occur from pressure of the tumors on vital organs. The disease probably belongs in the general group of lymphosarcoma. It is my opinion that the patient demonstrates the cutaneous manifestations associated with giant follicular lymphoblastoma.

In regard to the term chronic discoid lichenoid dermatitis, I may state that I believe such a term merely emphasizes the appearance of the lesions and conceals a lack of knowledge as to the cause of the disease. The picture is that which occurs in known general diseases like mycosis fungoides, leukemia and other internal diseases, or it may be the result of neurodermatitis. The use of this name may also discourage more careful studies in the attempt to detect the causal relation of cutaneous lesions to a general disease.

Dr. Frank C. Combes: In regard to the prognosis for patients with this condition, I do not think they all die; probably relatively very few of them die. I think if this man changed his environment his condition would improve, but it

is necessary to change the environment in order for him to get well. I have treated some patients with roentgen rays and there is some improvement, but this therapy is not as effective as a climatic change.

Pellagra. Presented by DR. TIMOTHY J. RIORDAN.

H. J., a Negress aged 31 was previously presented before the New York Dermatological Society, in November 1941 (this issue, page 1004).

DISCUSSION

DR. PAUL GROSS: I agree with the diagnosis but should like to take issue with the use of the word atypical for lesions of pellagra on the unexposed parts of the body. Friction, as present in the groin, vulva and submammary and intergluteal folds, and stretching of the skin, as over the elbows, knees and coccyx, may precipitate a pellagrous dermatitis, as does exposure to sunlight. These lesions are seen particularly in the so-called wet pellagra. I should be interested to know whether this patient has been examined for vitamin A deficiency, since she shows lesions on the conjunctiva which are suggestive of that condition.

DR. MAURICE J. COSTELLO: I have had an opportunity at Bellevue Hospital to observe a considerable number of patients suffering with pellagra. They certainly have not had lesions other than on the exposed parts, such as the face, the backs of the hands, the feet and the V of the chest. The cutaneous lesions are sometimes associated with lesions of the mucous membranes and psychic disturbances. I present this patient tonight because I think her condition is unusual. I do not think nicotinic acid is an essential part of the therapy, because most of the patients improve promptly on Bellevue Hospital fare. Most of the patients are men, and all or most of them give a history of imbibing freely of impure alcohol for a long time without intake of sufficient food.

DR. DAVID BLOOM: This case illustrates that the factor of sunlight is unnecessary for the production of cutaneous pellagra. In all the cases I have observed the eruption developed in the spring and there was a history of both ingestion of excessive alcohol and exposure to sunlight.

DR. E. WILLIAM ABRAMOWITZ: Several interesting points have been raised here. Some think that an eruption of pellagra is unusual on the unexposed parts, and some think it is not. I have seen pellagra on the unexposed parts. Spies is not convinced that exposure to sunlight is an important factor in producing the eruption of pellagra. It is fair to assume that when pellagra develops there are other vitamin deficiencies present. This patient should not be treated with nicotinic acid alone but with all the vitamins, minerals and a high calory diet, particularly to prevent "beriberi heart."

DR. LOUIS TULIPAN: In 1927 Maloney and I reported 21 cases of alcoholic pellagra that we observed during one summer. In every one of them there was an eruption either on the extensor surfaces of the hands or in the mouth. I think one patient had lesions on the feet and another around the eyes. In other words, they never showed the eruption on any other parts of the body and all got well on hospital fare within a week. They were not given vitamins at any time. No patients showed mental symptoms except 2, who had delirium tremens. This was during prohibition, and in all these cases the pellagra may have been due to drinking impure alcohol.

DR. FRANK C. COMBES: This case impressed me as being unusual. Edward Jenner Wood, who has probably seen more pellagra than any one else, reported thousands of cases in North Carolina, and in not one of them did he describe the location of the eruption as in this case. The nearest approach was in a case in which a man had lesions on the scrotum. But he did say he noticed that every patient who presented lesions on the hands and feet invariably had some lesions on the body.

DR. TIMOTHY J. RIORDAN: In regard to Dr. Bloom's question about seasonal incidence, I believe this is the third case I have observed in which lesions have occurred in the winter or late fall.

Papulonecrotic Tuberculid. Presented by DR. M. J. COSTELLO.

E. B., a man aged 61, was previously presented by Dr. Frank C. Combes before the New York Dermatological Society, on Nov. 25, 1941 (this issue, page 1008).

DISCUSSION

DR. EUGENE F. TRAUB: When this patient was previously presented I was alone in suggesting another diagnosis. The lesions on the legs particularly suggested parapsoriasis varioliformis acuta to me, but perhaps some of the members did not have the opportunity to look at these lesions very well. The age of the patient, the sudden onset about six weeks ago and the fact that the earliest lesion was a vesicle rather than a hard papule, with some lesions later becoming hemorrhagic or pustular and terminating either in necrosis or scaling, all seem to suggest parapsoriasis varioliformis acuta.

DR. PAUL GROSS: On the extensor surfaces of the forearms can be seen small lichenoid lesions, which were described many years ago by Wallhauser, of Newark, as typical of pityriasis lichenoides. In addition, there is a polymorphous eruption with varying degrees of exudative changes which accounts for the picture of parapsoriasis varioliformis.

DR. FRED WISE: The clinical features appear to be more in favor of parapsoriasis varioliformis than of papulonecrotic tuberculid.

DR. CHARLES WOLF: The unusual feature is the multiplicity of these lesions, with vesicular, crusted, slightly gangrenous lesions on the palms. And this, whether or not the patient had it two weeks ago, should have given a clue. Tuberculids rarely, if ever, appear on the palms; occasionally the backs of the hands and fingers show lesions.

DR. OSCAR L. LEVIN: I do not believe a positive diagnosis has been made in this case. When I first saw the patient I thought he had parapsoriasis varioliformis. However, there were peculiar hemorrhagic, well defined, vesicular lesions on the palms. I have not seen lesions of this type except in cases of generalized infections, such as gonococcemia and meningococcemia. I think the patient should be studied for the possibility of tuberculosis somewhere in the body. All of the lesions can be explained on the basis of tuberculosis.

DR. EUGENE F. TRAUB: I should like to emphasize one other point: This man has pulmonary tuberculosis which became evident twenty years ago. According to the literature, papulonecrotic tuberculid is rather rare in cases of clinically evident pulmonary tuberculosis.

DR. DAVID BLOOM: I have observed at least 2 cases of parapsoriasis varioliformis in which there were numerous vesicular lesions on the palms.

DR. MAURICE J. COSTELLO: I think that in spite of previous discussions I shall be forced to stand by the diagnosis of papulonecrotic tuberculid for the following reasons: The man has pulmonary tuberculosis, which was preceded by this eruption; syphilis developed, and during the course of antisyphilitic treatment the eruption disappeared. The eruption is generalized and symmetric, appears in crops and leaves punched-out scars on the elbows and knees which are characteristic of papulonecrotic tuberculid. There is no constitutional reaction. He has a hypersensitivity to tuberculin, giving positive reactions to a dilution of 1:100,000 and of 1:1,000,000, which is usually seen. The statement has been made that papulonecrotic tuberculid does not occur in pulmonary tuberculosis. I think one of the criteria of papulonecrotic tuberculid is the fact that patients who have it

give a history of having had pulmonary tuberculosis or later the disease develops in them. I have at present in Bellevue Hospital 3 or 4 patients who have both pulmonary tuberculosis and papulonecrotic tuberculid, and I have seen at least half a dozen other patients of whom this has been true. Papulonecrotic tuberculids and erythema induratum are the most frequent types of tuberculosis of the skin seen in those suffering from pulmonary tuberculosis.

A Case for Diagnosis (Tertiary Syphilis?). Presented by DR. LOUIS TULIPAN.

M. F., a white man aged 32, referred by Dr. Irving Shapiro, has suffered from pains in the joints, cutaneous nodules and inflammation of first the left eye and then the right eye, with loss of vision in the left eye, gradually progressing during the past twelve years.

The patient had submaxillary swellings at 18 years of age and pneumonia at 29. A cough persisted for one year. About six weeks ago the right eye became inflamed again, and two weeks ago, the left eye.

The patient presents pea-sized violaceous nodules arranged in plaques on the elbows. These leave scars on healing. There are also nodules in arciform arrangement on the thigh and numerous others scattered over the both legs, with scarring.

The Kahn and Hinton reactions of the blood were negative, and the results of urinalysis and the red blood cell count were within normal limits. The results of chemical examination and the sedimentation rate of the blood were normal. Prostatic smears were negative for gonococci. The reaction to a Vollmer patch test was 2 plus in forty-eight hours. Fluoroscopic examination of the lungs, hands and feet showed no abnormalities.

The ophthalmologist's diagnosis was iridocyclitis with inflammation of the uveal tract. Tuberculosis of the eye was said to be absent.

DISCUSSION

DR. IRVING SHAPIRO (by invitation): Biopsies of tissue from the lesions of the arm and leg showed obliterative endarteritis, some collagen degeneration and small and large round cell infiltration, suggesting syphilis. In spite of this report, I should like to suggest a diagnosis of sarcoid, in view of the fact that the patient has had an iridocyclitis of many years' duration.

DR. PAUL GROSS: The histologic report does not permit a diagnosis of sarcoid, but the clinical picture with the cutaneous lesions and the presence of uveitis is strongly suggestive of sarcoidosis. Quantitative intradermal tuberculin tests would be preferable to the tuberculin patch test in order to ascertain the degree of allergy or anergy present.

DR. H. VICTOR MENDELSOHN: I have no definite opinion on the diagnosis, but I wish to make a brief comment on the tuberculin patch test (Vollmer). In my opinion this test has no diagnostic value in dermatology. Recently I applied the test to a group of about 50 patients with various dermatoses, including a small number with different types of cutaneous tuberculosis and tuberculids. The reactions (eczematous) were strongly positive in all patients above the age of 18 years. The strongest reactions were seen in those who were free from cutaneous tuberculosis. A negative reaction was obtained in 2 children below the age of 5 years. As Dr. Gross pointed out, tuberculin sensitivity should have been determined by the Mantoux method, employing graded dilutions of old tuberculin.

DR. WILLIAM DIRECTOR (by invitation): I showed the histologic section to some general pathologists, who agreed that the disease was not sarcoid, syphilis or tuberculosis. The slide showed pronounced perivasculitis, large and small round cells, some areas of obliterative endarteritis throughout the whole extent of the corium and areas of collagen degeneration, with plasma cells in the infiltrate.

DR. DAVID BLOOM: The peculiar-looking plaques below the elbows suggest to me some lipoid abnormality of the skin.

A Case for Diagnosis (Lymphangioma of the Tongue with Fibrosis?). Presented by Dr. Girsch D. Astrachan.

T. M., a white man aged 22, first consulted me on Nov. 22, 1941 and gave a history of having had an abnormal condition of the tongue as far back as he could remember. Occasionally, from some trauma, such as biting or scratching with the toothbrush, the tongue becomes bluish and irritated and will bleed easily. On these occasions the patient experiences a stinging sensation when eating or drinking.

On the right side of the anterior part of the tongue there is a hazelnut-sized, well defined, slightly elevated, somewhat indurated lesion involving almost the entire structure of this part of the tongue. The surface of the lesion is partly verrucous and partly soft and presents several pinhead-sized and smaller deeply seated vesicles, a few reddish-bluish spots and a few eroded areas.

The Wassermann reaction of the blood was negative, and urinalysis and a complete blood count gave essentially normal results.

DISCUSSION

Dr. E. William Abramowitz: One of the things that Dr. Astrachan wants is some suggestion as to treatment. I suggest a sclerosing solution—either invert sugar or quinine hydrochloride.

Dr. Eugene F. Traub: I believe the induration comprising the base of the lesion is probably due to fibrosis, as Dr. Astrachan suggested. It is certainly not a malignant process, and I agree with the diagnosis as presented. As far as treatment is concerned, I am not certain that sclerosing solutions would destroy this lesion unless one were fortunate enough to sclerose a large central vessel. Lymphangiomas are made up of tiny separate vessels and are usually harder to destroy than the raised or deep vascular nevi. I suggest using an electric cutting current or actual cautery and shaving the surface of the lesion, perhaps more than once. If done as thoroughly as possible on the first occasion, one treatment might suffice. Treatment should be given not only to the dorsal surface of the tongue but to the under surface.

Dr. Charles Lerner: In my opinion the hardness is due to scar tissue, resulting from repeated injury to the tongue by the patient himself, either in chewing or in accidentally biting it. Tissue of this type, as a rule, is vulnerable. Regarding therapy, I do not believe that radium will be of much avail in this case. Lymphangiomas and hemolymphangiomas, particularly the adult type, do not respond readily to radium; in infants the response is much better. The best result in this case, in my opinion, could be obtained by electrolysis, inserting the needle into each lymph nodule or vesicle. It is, of course, a slower process than electrocoagulation, but the result is apt to be much better. I should hesitate to use sclerosing solutions because of the danger of sloughing and infection in the mouth.

Dr. Girsch D. Astrachan: This case was presented because I was unable to explain the cause for the fibrosis. I agree with Dr. Lerner that this could be explained by the continuous trauma and irritation.

Mosaic Warts After Treatment. Presented by Dr. Andrew H. Montgomery and Dr. Royal M. Montgomery.

A. S., an Austrian woman aged 45, was presented before this society on Oct. 7, 1941 (Arch. Dermat. & Syph. **45**:619 [March] 1941), with an extensive invasion of resistant, patchy warts. In addition, there were single and compound lesions scattered about the toes.

After seven weeks' treatment the mosaic warts have disappeared completely. There are no scars or other signs of the previous disease. Treatment included the

conjoint use of daily inunctions of 60 per cent salicylic acid paste and occasional applications of a strong solution of silver nitrate. No roentgen therapy has been given.

DISCUSSION

Dr. E. William Abramowitz: I congratulate the Drs. Montgomery on the excellent results in this case. I should like to have more details of the treatment.

Fig. 1.—Mosaic warts before treatment.

Dr. Frank C. Combes: I also wish to congratulate the Drs. Montgomery on this result. I have followed their technic and have invariably gotten excellent results with 60 per cent salicylic acid paste and silver nitrate.

Dr. Andrew H. Montgomery: This patient had very little treatment with silver nitrate. We applied 60 per cent salicylic acid paste covered by adhesive plaster. It was left on for two days, and then she removed the dressing and rubbed in 30 per cent nightly with the knobbed end of a clothes pin. We saw her once a week.

There was a little objection two months ago to our warning against the use of roentgen therapy for this disease. Less than a month ago we had a patient with large mosaic warty patches on the ball of the big toe. That patient had had altogether fifteen roentgen ray treatments by two excellent therapeutists, and there was an area of erythema present when we saw her. I think she had a real radio-

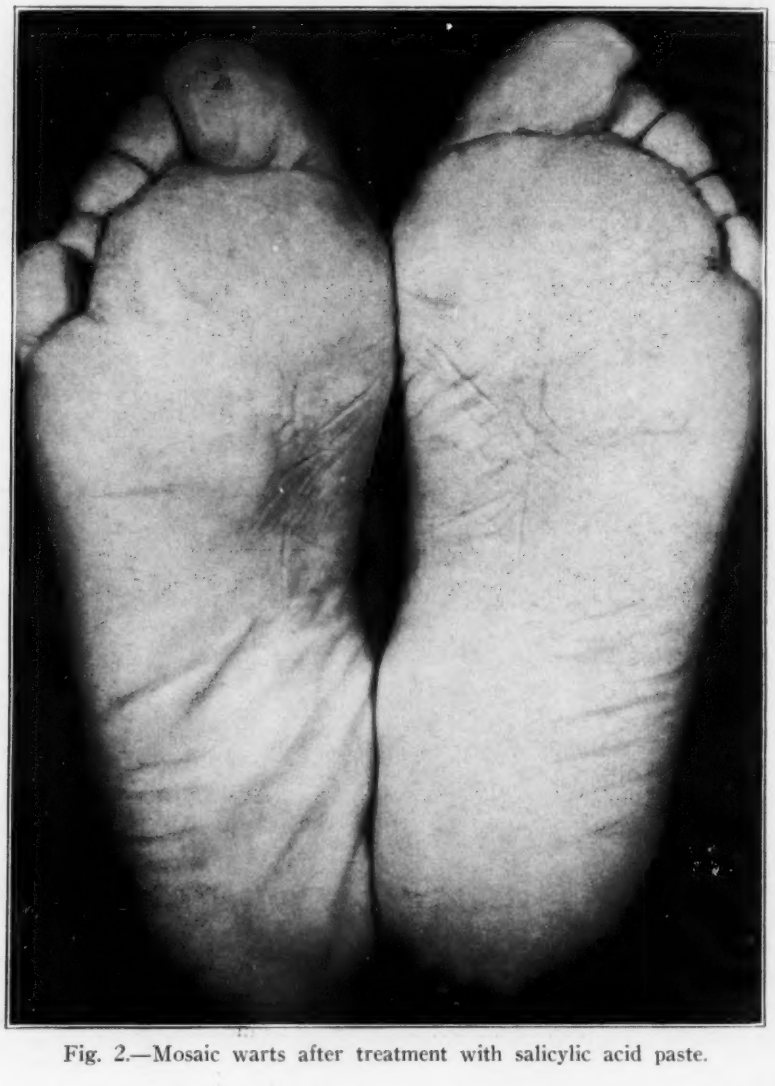

Fig. 2.—Mosaic warts after treatment with salicylic acid paste.

dermatitis. One does not see erythema or any inflammatory edema around ordinary mosaic warts. I merely want to warn again against the use of roentgen rays for this type of warts. They usually respond to salicylic acid.

Familial Bullous Dyskeratosis (Familial Benign Chronic Pemphigus [Hailey and Hailey]). Presented by Dr. E. N. Boccanegra Lopez.

A. D. P., a white Puerto Rican woman aged 38, is presented with an eruption which began eleven years ago, soon after a complicated delivery of twins. Two

younger brothers and an older sister have similar eruptions, the youngest at 21 and the oldest at 26. The patient has three children; a son has occasional herpes labialis, and the youngest child, a girl aged 3, has suffered from eczema since early life and is still under treatment.

The patient presents active lesions in the axillas, beneath the breasts and in the upper parts of the abdominal and crural regions. There is residual pigmentation on the sides of the neck at the site of former lesions, together with small atrophic leukodermic spots.

A complete physical examination reveals nothing abnormal aside from the cutaneous lesions. Her health is apparently unaffected by the condition. The Wassermann reaction of the blood was negative, and the blood count and the results of urinalysis were within normal range.

A Vollmer patch test elicited a positive reaction with a delayed "follicular type" of reaction one week after, which was still visible on the left arm after five weeks. The test provoked a severe systemic reaction with fever, sweating, pain in the joints and bones and the appearance of typical subcutaneous nodules of erythema nodosum, coming in crops for three weeks after the tuberculin test. At the site of the test erythema-multiforme-like vesicular lesions were observed, and on each forearm at about the upper third on the extensor surface there were erythema-multiforme-like lesions.

Trichophytin and oidiomycin tests (1:100 dilution) elicited 2 plus and 1 plus reactions respectively.

Direct mycologic examination of scales, crusts, pus and fluid from the lesions gave negative results. Cultures on Sabouraud mediums were likewise negative.

Nikolsky's sign was positive on the back of the neck. Specimens for biopsy were taken from the left axilla and the upper part of the left side of the abdomen just below the left breast. Examination showed intraepidermal vesicles, acanthosis with projection into the cutis by the papillary layer and some pigmentation with a low grade chronic inflammatory reaction, particularly around some of the small vessels. The diagnosis was pemphigus.

The patient has been treated with moccasin venom in increasing doses, beginning with 0.1 cc. and doubling the dose; she is now getting 1 cc. every five days and shows great improvement after two weeks.

The points in clinical diagnosis are: 1. The disease appears in the second decade of life in either sex. 2. The extreme chronicity of the disease is not influenced by any treatment known, up to this time. 3. The patient enjoys comparatively good health except during the acute episodes every six or eight months, when there is much itching with a flare-up of lesions. 4. There is coincidental appearance of the disease in other members of the family; the disease seems to be transmitted by a recessive gene, as not all the members of the family show the syndrome.

DISCUSSION

DR. TIMOTHY J. RIORDAN: I saw the slide from this case yesterday, and the condition is definitely a bullous dermatitis. The section shows a large breach right through the epidermis, with the floor lined with basal cells and the roof broken through, but for the most part the epidermis is intact.

DR. E. WILLIAM ABRAMOWITZ: The disease looks like the familial benign chronic pemphigus of Hailey and Hailey. Epidermolysis bullosa hereditaria, according to Wise and Sulzberger, has some points in common with this dermatosis.

DR. FRED WISE: The features of this patient's eruption conform with those described by several authors, among them Pels, Goodman, Anderson and the Hailey brothers. The condition appears to be a form of familial, chronic and recurrent bullous dermatosis with certain clinical features simulating hereditary epidermolysis bullosa. In all the cases which have been reported, the histologic changes in the epidermis resembled those characterizing Darier's disease. In my opinion this does not justify the assumption that the dermatosis is a variety of keratosis follicularis of Darier. Various forms of dyskeratosis exist in several other dermatoses which bear no clinical relation to Darier's disease.

DR. TIMOTHY J. RIORDAN: There was no evidence of *corps ronds.* I did not mean to imply that I had made any diagnosis at all, other than that the condition was a fine example of a bullous eruption.

DR. EUGENE F. TRAUB: This disease is characterized by the presence of bullous and crusted lesions, and if enough sections are taken there is demonstrable a type of dyskeratosis not generally accepted as the dyskeratosis of Darier's disease yet suggesting that that possibility remains to be elucidated. In reporting these cases, I have proposed that one get away from the term pemphigus, which —although it means only "blister"—always suggests a bad prognosis. I suggested the designation "benign familial bullous dyskeratosis," which fairly accurately describes the disease and does not commit one to a specific causation.

Book Reviews

Cancer of Face and Mouth; Diagnosis, Treatment, Surgical Repair. By Vilray P. Blair, M.D., Sherwood Moore, M.D., and Louis T. Byars, M.D. Price, $10.00, cloth. Pp. 599, with 324 illustrations. St. Louis: C. V. Mosby Company, 1941.

The practitioner who has the time and the inclination to read the abundant literature dealing with cancer of the face and mouth (which includes most of the tissues above the shoulder girdle) must be aware of the diversified methods advocated by physicians for treatment. Take, for example, a cancer of the mucocutaneous portion of the lower lip. What is generally conceded to be "the best treatment?" Should it be with roentgen rays, interstitial radium seeds, actual cautery, electrodesiccation or scalpel surgery? Should there be a judicious combination of several or even of all modalities? What procedures are advocated as the most thorough and the safest with respect to the lymph nodes of the neck? Which technic is best for end results?

In this compact volume the answers to innumerable problems of similar portent are clearly and adequately presented. The diagnosis, prognosis, prophylaxis and treatment are set forth in simple and lucid style. The keen minds and sound judgment of the authors are reflected in every chapter. The meticulous attention to detail, in words as well as in illustrations, is an especially noteworthy feature of the book.

The book comprises nineteen chapters devoted to cancer of the external parts of the face (for instance, ear, nose, cheek and lips) and of the mouth, nasopharynx, nasal and orbital cavities, sinuses, maxillary antrums, salivary glands and neighboring structures. One short chapter deals with moles, nevi and malignant melanomas. In this chapter the reviewer notes with interest the following statement: "The hair-bearing mole, although distressing because of the deformity, has not in our experience ever been the site of a malignancy." Speaking of large moles which require surgical removal under favorable conditions, the authors state: "Removal must sometimes be done piecemeal; even when this involves cutting across such a mole, no ill effects have been observed." As is well known, not all dermatologists are inclined to subscribe to this view. The reviewer, too, has not encountered malignant changes in hairy moles.

The first three chapters are devoted to general considerations in the treatment of cancer of the mouth and face, the underlying principles of surgical destruction and removal of the cancer and the care of the patient.

One chapter deals with cervical node metastases and neck dissection; this is an exceedingly valuable and highly important part of the volume. The practitioner and the specialist whose knowledge of the significance of lymph node metastases is vague or, at best, incomplete will appreciate the significance of the initial sentence in this chapter: "An understanding surgeon never thinks of cancer as disassociated from potential lymphatic metastases."

Chapters 17, 18 and 19 are devoted respectively to anesthesia, destruction by irradiation and follow-up statistics. The last portion of the volume, comprising 207 pages, presents excellent free hand drawings of a multitude of operative technics. These drawings are in the form of "plates," all of which are accompanied by concise descriptive legends on the opposite pages. The large majority illustrate the many diversified and often complicated procedures in the art of plastic surgery and repair.

The text itself, 358 pages, is accompanied by 260 illustrations of clinical material and a number of roentgenograms of the bony structures of the face and head; these are excellent reproductions of photographs and are all accompanied by

explanatory and descriptive legends indicating the outstanding features of diagnosis, prognosis and therapy, as well as the end results after the lapse of months and years.

The selection of methods and procedures and the choice of different modalities best suited to the innumerable problems which confront the surgeon are clearly and succinctly described. These descriptions reflect the exceptionally broad and comprehensive experience of the authors individually and collectively; surgery, physical therapy, radiation therapy and pathology are discussed in detail, and the indications for the employment, in selected cases, of the knife, the actual cautery, electrodesiccation, radium, radon seeds, roentgen rays, etc.—separately and together —are clearly demonstrated throughout the volume.

Summed up, the structure of the subject as a whole rests on the essential desiderata applicable to cancer in general: (1) early recognition and treatment; (2) selection of a rational plan of treatment; (3) adequate execution of the selected plan, and (4) adequate observation and care of the patient before, during and after treatment.

The book is strongly recommended as a valuable addition to the libraries of practitioners, both general and specialistic.

Diseases of Women. By Dr. Harry Sturgeon Crossen, F.A.C.S., Professor Emeritus of Clinical Gynecology, and Dr. Robert James Crossen, Assistant Professor of Clinical Gynecology and Obstetrics, Washington University School of Medicine, St. Louis. Ninth edition. Price, $12.50. Pp. 896, with index, references and colored and black and white illustrations. St. Louis: C. V. Mosby Company, 1941.

The fact that this standard textbook has gone through nine editions since 1907 is strong evidence of its value. This reviewer is not in a position to discuss the major part of the book except to say that it has an unusual number of excellent illustrations, including clinical photographs, photomicrographs, charts and diagrams. Of these, 45 are in color.

The portion of the book of special interest to dermatologists (chapter IV) is entitled "Diseases of the External Genitals and Vagina" and consists of 93 pages. The first 12 pages of this chapter, the least important from the dermatologic standpoint, are devoted to gonorrhea. In the rest of the chapter are described: other types of vulvitis, other types of vaginitis, monilial vaginitis, atrophic vaginitis, ulcerative diseases, urethral conditions, vulvovaginal gland diseases, nonmalignant growths and swellings of the vulva, nonmalignant growths and swellings in the vagina, malignant disease of the vulva, malignant disease of the vagina and miscellaneous disturbances.

The sections on leukoplakia vulvae atrophica and trichomonas and monilial vaginitis are adequately discussed and well illustrated and should be of special interest to the dermatologist. The section on ulcerative diseases of the vulva and vagina, including, among other diseases, chancroid, syphilis, tuberculosis, granuloma inguinale and lymphogranuloma venereum, contain little that is new to the dermatologist. The discussion of diseases of the vulvovaginal glands includes abscess, sinusitis and tuberculosis and should interest the dermatologist, even though these diseases are usually seen and treated by the gynecologist. Both benign and malignant growths of the vulva are well described and profusely illustrated. Striking photographs of cancer of the vulvovaginal gland are included, showing extremely rapid growth during pregnancy. Among miscellaneous diseases the subject of pruritus vulvae is somewhat briefly discussed, the exciting causes being listed under ten headings.

A few minor criticisms could be made, such as the statement that the cause of the common wart is not known. Again, in speaking of the treatment of granuloma inguinale by intravenous injections of antimony and potassium tartrate, the authors state that "after three or four administrations . . . healing promptly follows." Such a statement could not be based on long experience with this disease.

The entire volume is printed on glazed paper on account of the numerous illustrations, which in general are most excellent, and the printing and general makeup of the book are all that could be desired. Nearly eight hundred bibliographic references are included.

The book is highly recommended to dermatologists.

La lepra en México. By Jesús González Urueña. Pp. 793, with 13 pages of indexes. Buenos Aires, Argentina: El Ateneo, 1941.

In a large volume Dr. Urueña reviews and classifies more than two hundred articles published mostly by Mexican authors concerning different aspects of leprosy in Mexico.

The importance of this study is evident. There were 5,145 cases of leprosy registered between 1936 and 1938. The author states that it would not be an exaggeration to consider that the number of cases might be as high as 15,000. Only Brazil and Colombia show a larger number of cases in this hemisphere.

The history from the days before the conquest, statistics, clinical descriptions, prognosis, diagnosis and treatment are extensively discussed.

Most interesting are the chapters on ocular manifestations and leprosy in children. A painstaking study is made of the prophylaxis, and the text of laws concerning the disease is given. The twenty-one dispensaries distributed over the country especially equipped for diagnosis and treatment are enumerated. The three leprosariums, at Pénjamo, Sarabia and Zoquiapam, are described in detail. These modern institutions occupy vast areas, and each consists of a large number of separate buildings. Many photographs and maps show how comfortable and well equipped they are.

In a separate chapter eleven different organizations caring for the welfare of the patients are mentioned. There are many photographs of pamphlets which are distributed to the public for its education in this disease.

In the chapter about treatment Dr. Urueña reviews about thirty articles covering practically all the therapeutic procedures recommended, except for the newly advocated diphtheria toxoid.

Worthy of mention is a careful study the author published with Dr. L. de J. Lozano about the failure of methylthionine chloride (methylene blue) in the treatment of leprosy.

It is gratifying to see the interest of Mexican physicians in this important subject. The large number of valuable studies on different aspects of the disease speak for themselves. It is time that more attention be paid to the scientific production of the Latin-American countries.

This book is an excellent example of how many interesting dermatologic articles published in this hemisphere have been almost entirely unknown in the United States, while the European publications have been attentively followed.

Dr. Urueña's book is of great merit, and those interested in this subject will find in it a valuable reference book where all the phases of the disease are thoroughly discussed.

The volume is cardboard bound, printed on paper of good quality and profusely illustrated.

Natural Resistance and Clinical Medicine. By David Perla and Jessie Marmorston. Price, $10.00. Pp. 1,298. Boston: Little, Brown & Company, 1941.

The difficult task of attempting to explain the importance of natural resistance of the host in determining the occurrence and outcome of infection has been undertaken by the authors. They distinguish between natural and acquired resistance. Acquired immunity depends on the presence of antibodies and on an altered state of the tissues in their reaction to reinfection. Natural resistance has for many years been attributed to differences in "constitution." It is now apparent that while heredity is a factor a definite part of the difference in "constitution" is due to

the functional activity of the glands of internal secretion. Recent knowledge in the field of nutrition, especially among the vitamins, shows these substances to be closely related to the hormones in many of their physiologic activities, including those related to natural resistance and susceptibility.

The book is arranged in ten sections. Among the subjects for these sections are the following: heredity and resistance; age and sex and resistance; the role of other endocrine glands in resistance; humoral and cellular mechanisms in resistance; the role of the liver, body surfaces and nervous system in resistance, and diet and climate and resistance. The sections are divided into chapters, each of which is summarized. At the end of each chapter is an extensive bibliography.

The authors are well aware of the many difficulties encountered in attempting to draw conclusions in the many phases of this subject. They have recognized that psychologic, mental and economic factors are of importance in influencing the resistance of a person to infection and are aware of the difficulty of exposing these to critical analysis. They have analyzed the recent knowledge concerning natural resistance and infection and have pointed out that through further advances one may improve the vigor and longevity of man, or, as Sherman has stated, ". . . add life to our years and years to our lives."

Our Sex Life. A Guide and Counsellor for Everyone. By Fritz Kahn, M.D. Translated from the German by George Rosen, M.D. Second revised edition. Pp. 459, with 41 illustrations. New York: Alfred A. Knopf, 1942.

This book is written in interesting and comprehensible language. It acquaints the reader with the anatomy and functions of the sex organs and with sex relation in its various aspects. The problems of fertility, sterility, birth control, abortion, prostitution and disturbances of sex life are discussed and treated intelligently.

Unfortunately, the value of the book is considerably lowered by the chapter on venereal diseases. The treatment of chancroid by iodoform is mentioned, but not with sulfanilamide and its derivatives. Numerous outdated and incorrect statements are made, some of which are as follows: Syphilis means probably mutilating disease. Large gummas disappear in a few days after arsphenamine therapy. Approximately one half of all epileptic fits during childhood have a syphilitic basis. Thirty per cent of all mentally inferior children provided for in institutions are syphilitic. Beethoven's deafness was due to hereditary syphilis, and he died at the age of 56 from hereditary syphilis. These are only a few of the incorrect statements made by the author, and they diminish the confidence of the reader in the remainder of the book, which is in the opinion of the reviewer of great value as a guide on sex life.